THIOSEMICARBAZONES AS ANTI-VIRALS AND IMMUNOPOTENTIATORS

[0001] This application claims benefit of priority to the following US Provisional Patent Applications, serial no. 60/436,472, filed December 27, 2002; serial no. 60/436,638, filed December 30, 2002; and serial no. 60/438,487 filed January 10, 2003; each of which is incorporated herein by reference in its entirety for any purpose.

FIELD OF THE INVENTION

[0002] This invention relates to compounds and compositions, as well as uses of the compounds as immunopotentiators and use of the compounds in methods for treating and preventing viral infections including HCV. More particularly, the invention relates to compounds that are used alone or combined with other agents for which the immune response is desired, in the treatment or modulation of cancer, allergic diseases, asthma, as well as amelioration of viral, bacterial, and fungal infections.

BACKGROUND OF THE INVENTION

[0003] It is known that immune response to certain antigens which are otherwise weakly immunogenic can be enhanced through the use of vaccine adjuvants. Such adjuvants potentiate the immune response to specific antigens and are therefore the subject of considerable interest and study within the medical community.

[0004] Research has permitted development of vaccines possessing antigenic epitopes that were previously impossible to produce. For example, currently available vaccine candidates include synthetic peptides mimicking streptococcal, gonococcal, and malarial antigens. These purified antigens are generally weak immunogens, however, that require adjuvants in order to evoke protective immunity. However, conventional vaccine adjuvants possess a number of drawbacks, which limit their overall use and effectiveness.

[0005] It is also common knowledge that substances, which stimulate immune cells in vitro exhibit similar immuno-stimulatory effects in vivo. These compounds, such as recombinant cytokines, pathogen products (e.g. toxins, lipids, proteins/peptides, carbohydrates and nucleic acids) and other mammalian-derived immunostimulatory molecules (e.g. heat shock proteins, complement, immune complexes and proteoglycans) all induce a measurable pro-inflammatory response both in vitro and in vivo.

[0006] Historically, the classic adjuvants have been Freund's complete or incomplete (i.e., without mycobacteria) adjuvants. Edmund Coley, the inventor of Coley's Toxin, described this potential for cancer immuno-therapy.

[0007] Other adjuvants have been compared to Freund's. However, clinical use of such adjuvants in animals or humans is precluded because they produce granulomas at the site of injection; fever and other toxic effects; and tuberculin hypersensitivity. Other materials, such as mineral oil and aluminum hydroxide, have also been used as adjuvants, but they invariably suffer from disadvantages. For example, mineral oil is known to produce tissue irritation and to be potentially oncogenic. Aluminum hydroxide, the only approved adjuvant in the United States, also induces granulomas at the inoculation site and furthermore it does not effectively induce cell-mediated immunity. Moreover, many of the adjuvants currently available have limited utility because they contain components, which are not metabolizable in humans. Additionally, most adjuvants are difficult to prepare in that they may require time consuming procedures and the use, in some cases, of elaborate and expensive equipment to formulate a vaccine and adjuvant system.

[0008] For a thorough discussion of various immunological adjuvants, see "Current Status of Immunological Adjuvants", Ann. Rev. Immunol., 1986, 4, pp. 369-388, and "Recent Advances in Vaccine Adjuvants and Delivery Systems" by Derek T O'Hagan and Nicholas M. Valiente, both of which are hereby incorporated by reference in its entirety. See also U.S. Pat. Nos. 4,806,352; 5,026,543; and 5,026,546 for disclosures of various vaccine adjuvants appearing in the patent literature all of which are hereby incorporated by reference in its entirety.

[0009] There has been an effort to find new adjuvants for vaccines that would overcome the drawbacks and deficiencies of conventional adjuvants. In particular, an adjuvant formulation which elicits potent cell-mediated and humoral immune responses to a wide range of antigens in humans and domestic animals, but lacking the side effects of conventional adjuvants, such as Freund's complete adjuvant, would be highly desirable.

[0010] It is also desirable to identify small molecules, which stimulate a proinflammatory response for use as vaccine adjuvants.

[0011] Hepatitis is a systemic disease, which predominantly affects the liver. The disease is typified by the initial onset of symptoms such as anorexia, nausea, vomiting, fatigue, malaise, arthralgias, myalgias, and headaches, followed by the onset of jaundice.

The disease may also be characterized by increased serum levels of the aminotransferases AST and ALT. Quantification of these enzymes in serum indicates the extent of liver damage.

[0012] There are five general categories of viral agents which have been associated with hepatitis: the hepatitis A virus (HAV); the hepatitis B virus (HBV); two types of non-A, non-B (NANB) agents, one blood-borne (hepatitis C) and the other enterically transmitted (hepatitis E); and the HBV-associated delta agent (hepatitis D).

[0013] There are two general clinical categories of hepatitis, acute hepatitis and chronic hepatitis. Symptoms for acute hepatitis range from asymptomatic and non-apparent to fatal infections. The disease may be subclinical and persistent, or rapidly progress to chronic liver disease with cirrhosis, and in some cases, to hepatocellular carcinoma. Acute hepatitis B infection in adult Caucasians in the United States progresses to chronic hepatitis B in about 5% to 10% of the cases. In the remainder of the cases, approximately 65% are asymptomatic. In the Far East, infection is usually perinatal, and 50% to 90% progress to the chronic state. It is likely that the different rates of progression are linked to the age at infection rather than genetic differences in the hosts. In the United States, about 0.2% of the population is chronically infected, with higher percentages in high-risk groups such as physicians, drug addicts and renal dialysis patients. In countries such as Taiwan, Hong Kong and Singapore, the level in the population with hepatitis infection may be as high as 10%.

[0014] In the United States, about 20% of patients with chronic hepatitis die of liver failure, and a further 5% develop hepatitis B-associated carcinoma. In the Far East, a large percentage of the population is infected with HBV, and after a long chronic infection (20 to 40 years), approximately 25% of these will develop hepatocellular carcinoma.

[0015] After the development of serologic tests for both hepatitis A and B, investigators identified other patients with hepatitis-like symptoms, and with incubation periods and modes of transmission consistent with an infectious disease, but without serologic evidence of hepatitis A or B infection. After almost 15 years, the causative agent was identified as an RNA virus. This virus (designated "hepatitis C") has no homology with HBV, retroviruses, or other hepatitis viruses.

[0016] Hepatitis C (HCV) appears to be the major cause of post-transfusion and sporadic non-A, non-B (NANB) hepatitis worldwide, and plays a major role in the development of chronic liver disease, including hepatocellular carcinoma (Kuo et al., Science

244:362-364, 1989; Choo et al., British Medical Bulletin 46(2):423-441, 1990). Of the approximately 3 million persons who receive transfusions each year, approximately 150,000 will develop acute hepatitis C (Davis et al., New Eng. J. Med. 321(22):1501-1506, 1989). In addition, of those that develop acute hepatitis C, at least one-half will develop chronic hepatitis C.

[0017] Until recently, no therapy has proven effective for treatment of acute or chronic hepatitis B or C infections, and patients infected with hepatitis must generally allow the disease to run its course. Most anti-viral drugs, such as acyclovir, as well as attempts to bolster the immune system through the use of corticosteroids have proven ineffective (Alter, "Viral hepatitis and liver disease," Zuckerman (ed.), New York: Alan R. Liss, pp. 537-42, 1988). Some anti-viral activity has been observed with adenosine arabinoside (Jacyna et al., British Med. Bull. 46:368-382, 1990), although toxic side effects, which are associated with this drug render such treatment unacceptable.

[0018] One treatment that has provided some benefit for chronic hepatitis B and C infections is the use of recombinant alpha interferon (Davis et al., New Eng. J. Med. 321(22):1501-1506, 1989; Perrillo etal., New Eng. J. Med. 323:295-301, 1990). However, for patients with hepatitis B infections only about 35% of infectees responded to such treatment, and in perinatal infectees only about 10% responded to treatment. For hepatitis C infections, despite apparent short-term success utilizing such therapy, six months after termination of treatment half of the patients who responded to therapy had relapsed. In addition, a further difficulty with alpha interferon therapy is that the composition frequently has toxic side effects such as nausea, and flu-like symptoms, which require reduced dosages for sensitive patients.

[0019] A disease related to hepatitis B and hepatitis C infections is hepatocellular carcinoma. Briefly, hepatocellular carcinoma is the most common cancer worldwide. It is responsible for approximately 1,000,000 deaths annually, most of them in China and in sub-Saharan Africa. There is strong evidence of an etiologic role for hepatitis B infection in hepatocellular carcinoma. Carriers of the HBV are at greater than 90 times higher risk for the development of hepatocellular carcinoma than noncarriers. In many cases, hepatitis B virus DNA is integrated within the cellular genome of the tumor. Similarly, hepatitis C virus has also recently been found to be associated with hepatocellular carcinoma, based upon the observation that circulating HCV antibodies can be found in some patients with

hepatocellular carcinoma. At present, surgical resection offers the only treatment for hepatocellular carcinoma, as chemotherapy, radiotherapy, and immunotherapy have not shown much promise (Colombo et al., Lancet 1006-1008, 1989; Bisceglie et al., Ann. of Internal Med. 108:390-401, 1988; Watanabe et al., Int. J. Cancer 48:340-343, 1991; Bisceglie et al., Amer. J. Gastro. 86:335-338, 1991).

[0020] Therefore, therapeutics that could serve to augment natural host defenses against hepatitis, or against tumor induction and progression, with reduced cytotoxicity, or that allows treatment of interferon non-responsive individuals would be very beneficial. The present invention provides such therapeutic agents, and further provides other related advantages.

BRIEF SUMMARY OF THE INVENTION

[0021] The invention provides novel immune potentiators, novel vaccine adjuvants, novel compounds and pharmaceutical compositions, novel methods for treating viral infections, including HCV, by administering the compounds, and novel methods for modulating the immune response by administering the compounds.

The compounds used in the methods and compositions of the invention are small molecules. They have greater potential for finer specificity thus providing improved efficacy and safety profiles compared to existing immuno-stimulants and antivirals.

As adjuvants, the compounds are combined with numerous antigens and delivery systems to form a final vaccine product.

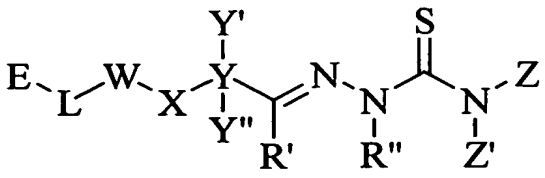
[0022] As immuno-therapeutics, the compounds are used alone or combined with agents or other therapies for which the immune response is desired for treatment or modulation of cancer, allergic diseases, asthma, and chronic infections such as coronavirus, SARS-associated coronavirus (SARS-CoV), HIV, HCV, HBV, HSV, and H. pylori.

[0023] One embodiment of the invention is a composition comprising:

[0024] a vaccine in an amount effective to stimulate a cell-mediated immune response; and

[0025] a vaccine adjuvant comprising a thiosemicarbazone or derivative thereof, in an amount effective to potentiate the cell-mediated immune response to the vaccine.

[0026] In another embodiment, the invention is an composition according to claim 1, wherein the thiosemicarbazone is a compound of formula I:



I

[0027] wherein:

[0028] E is absent or selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, heteroaryl, and substituted heteroaryl;

[0029] L is absent or is selected from the group consisting of oxo, amino, alkylene, substituted alkylene, alkoxy, alkylamino, aminoalkyl, heterocyclyl, carbocyclyl, and carbonyl;

[0030] W is absent or selected from the group consisting of cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, heteroaryl, and substituted heteroaryl;

[0031] X is absent or is selected from the group consisting of oxo, amino, alkylene, substituted alkylene, alkoxy, alkylamino, aminoalkyl, heterocyclyl, carbocyclyl, and carbonyl;

[0032] Y is selected from the group consisting of cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, heteroaryl, and substituted heteroaryl;

[0033] Y' is absent or is selected from the group consisting of F, Cl, Br, I, nitro, alkyl, substituted alkyl, and optionally substituted heterocyclyl, amino, alkylamino, dialkylamino;

[0034] Y" is absent or is selected from the group consisting of F, Cl, Br, I, nitro, alkyl, substituted alkyl, and optionally substituted heterocyclyl, amino, alkylamino, dialkylamino;

[0035] R' is H, alkyl, or substituted alkyl;

[0036] R'' is H, or

[0037] R' and R'' are taken together to form a hetercyclic ring;

[0038] Z and Z' are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, alkoxy, substituted alkoxy,

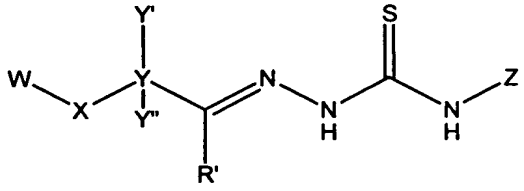
aminocarbonyl, alkoxycarbonyl, carboxyl sulfonyl, methanesulfonyl, and substituted or unsubstituted alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, heteroarylcarbonyloxy, heteroaralkylcarbonyloxy, alkylaminocarbonyloxy, arylamino-carbonyloxy, formyl, loweralkylcarbonyl, loweralkoxycarbonyl, aminocarbonyl, aminoaryl, alkylsulfonyl, sulfonamido, aminoalkoxy, alkylamino, heteroarylamino, alkylcarbonylamino, alkylaminocarbonylamino, arylaminocarbonylamino, aralkylcarbonylamino, heteroarylcarbonylamino, arylcarbonylamino, cycloamidino, cycloalkyl, cycloimido, arylsulfonyl and arylsulfonamido; or

[0039] Z and Z' are taken together to form a heterocyclic group, which may be optionally substituted;

[0040] the tautomers and the pharmaceutically acceptable salts, esters, or prodrugs thereof.

[0041] Other embodiments include methods of treating a viral infection comprising the step of administering to a subject a composition as described above.

[0042] Still other embodiments include a method of treating a viral infection or potentiating a cell-mediated immune response comprising administering to a subject a compound of formula II:



II

[0043] wherein:

[0044] W is selected from substituted and unsubstituted aryl, or a substituted and unsubstituted heteroaryl group having one ring or two fused rings;

[0045]

[0046] X is absent or is selected from the group consisting of oxo, amino, alkylene, substituted alkylene, alkoxy, alkylamino, aminoalkyl, heterocyclyl, and carbocyclyl, wherein if X is absent, Y and W together form an optionally substituted aryl or heteroaryl group having at least two fused rings;

[0047] Y is selected from substituted and unsubstituted aryl, or a substituted and unsubstituted heteroaryl group having one ring or two fused rings;

[0048] Y' is absent or is selected from the group consisting of F, Cl, Br, I, nitro, alkyl, substituted alkyl, and optionally substituted heterocyclyl, amino, alkylamino, dialkylamino;

[0049] Y" is absent or is selected from the group consisting of F, Cl, Br, I, nitro, alkyl, substituted alkyl, and optionally substituted heterocyclyl, amino, alkylamino, dialkylamino;

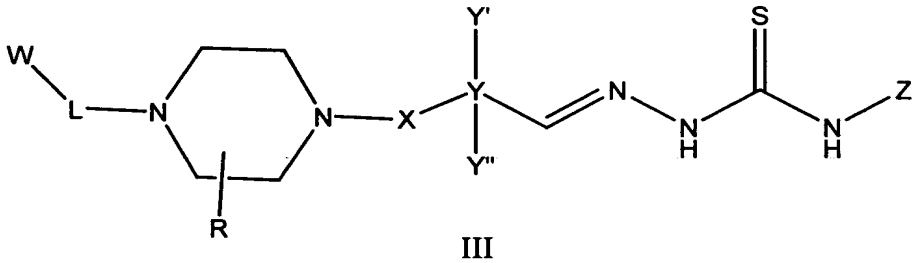
[0050] R' is H or CH_3,

[0051] Z is selected from the group consisting of hydrogen, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, and optionally substituted heterocyclylalkyl;

[0052] salts, prodrugs, or tautomers thereof.

[0053] Still other embodiments include compounds of formula III,

[0054]



III

[0055] wherein:

[0056] W is selected from the group consisting of substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heterocyclyl, and substituted or unsubstituted heteroaryl groups;

[0057] X and L are each independently absent or independently selected from the group consisting of lower alkyl and carbonyl;

[0058] R is absent or selected from the group consisting of carbonyl, amino, alkyl, substituted alkyl, alkylamino, and dialkylamino;

[0059] Y is an aryl or heteroaryl group;

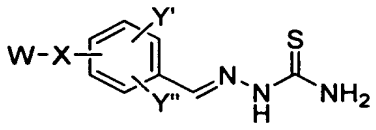
[0060] Y' is absent or selected from the group consisting of F, Cl, Br, I, alkyl, substituted alkyl, heterocyclyl, amino, alkylamino, dialkylamino, and nitro;

[0061] Y" is absent or selected from the group consisting of F, Cl, Br, I, alkyl, substituted alkyl, heterocyclyl, amino, alkylamino, dialkylamino, and nitro;

[0062] Z is hydrogen, or if Y is furanyl, then Z may be selected from the group consisting of alkyl, substituted alkyl, heterocyclyl, amino, alkylamino, dialkylamino, and nitro; and

[0063] salts, prodrugs, or tautomers thereof.

[0064] Yet other embodiments include compounds of formula IV,



IV

[0065] wherein:

[0066] W is an optionally substituted phenyl or pyridinyl group;

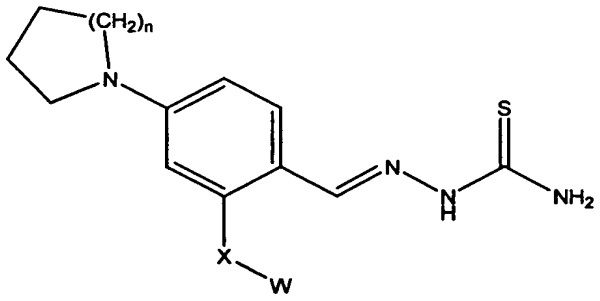
[0067] X is alkoxy or alkylamino;

[0068] Y' is H or fluoro;

[0069] Y' is dialkylamino, fluoro, or nitro; and

[0070] salts, prodrugs, or tautomers thereof.

[0071] Another embodiment includes compounds of Formula IVc



IVc

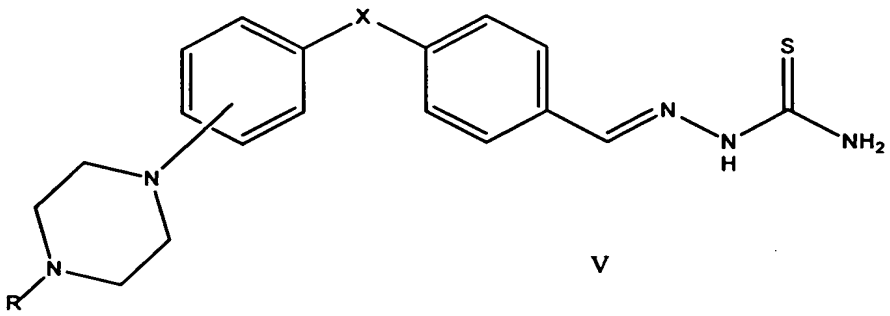
[0072] wherein:

[0073] W is phenyl substituted with at least one member selected from the group consisting of –Cl; -F; -Br; -CF3; -OCH_3; -NO_2; -CH_3; $N(CH_3)_2$; and –OCF_3;

[0074] X is alkoxy; and

[0075] n is an integer from 1 and 3.

[0076] Another embodiment includes compounds of Formula V



V

[0077] wherein:

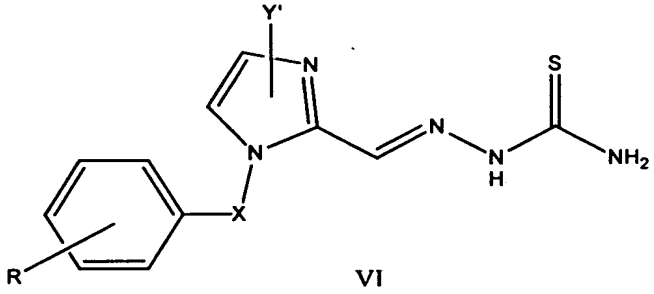
[0078] R is an alkyl group;

[0079] X is alkoxy; and

[0080] salts, prodrugs, or tautomers thereof.

[0081]

[0082] Still another embodiment includes compounds of Formula VI



VI

[0083] wherein:

[0084] X is absent or an alkylene;

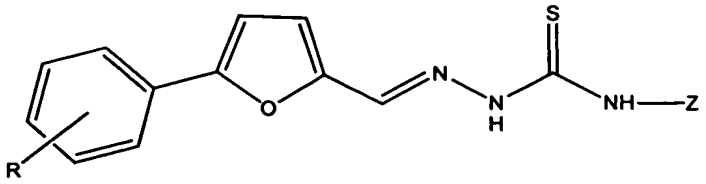
[0085] Y' is absent or is an alkyl group; and

[0086] R is a halogen; and

[0087] salts, prodrugs, or tautomers thereof.

[0088] Another embodiment includes compounds of Formula VII

[0089]



VII

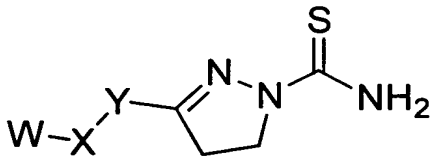
[0090] wherein:

[0091] R is nitro and Z is H; or

[0092] R is Cl and Z is selected from the group consisting of alkyl, pyridylalkylene, piperidinylalkylene, morpholinylalkylene, and piperizinylalkylene ; and

[0093] salts, prodrugs, or tautomers thereof.

[0094] Other embodiments include compounds of formula VIII and salts, prodrugs, or tautomers thereof:



VIII

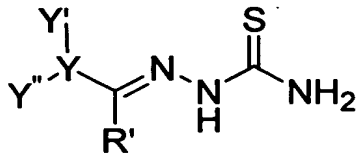
[0095] wherein:

[0096] W is a phenyl, substituted phenyl, pyridinyl, or substituted pyridinyl group;

[0097] X is absent or is selected from the group consisting of oxo, amino, alkylene, and substituted alkylene; and

[0098] Y is an aryl or heteroaryl group.

[0099] Another embodiment includes compounds of formula IX:



IX

[0100] wherein;

[0101] Y is an aryl or heteroaryl group having one ring or two fused rings;

[0102] Y' is selected from the group consisting of halo, nitro, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, heterocyclyl, substituted heterocyclyl, amino, alkylamino, and dialkylamino; and

[0103] Y" is absent or is selected from the group consisting of halo, nitro, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, amino, alkylamino, and dialkylamino.

[0104] Yet another embodiment includes pharmaceutical.

[0105] Another embodiment includes a method of treating a viral infection comprising administering to a subject a pharmaceutical composition composition comprising a therapeutically effective amount any of the above-mentioned compounds, salts and tautomers thereofe, and a pharmaceutically suitable carrier.

[0106] In some embodiments, the viral infection is HCV.

[0107] Some embodiments involve a method of treating viral infections in a subject comprising administering to the subject any one or more of the compounds described herein or, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer.

[0108] Still other embodiments involve the methods described above wherein the infection is an HCV infection.

[0109] Some embodiments of a method of adminstering a vaccine comprise simulatneously administering a vaccine in an amount effective to stimulate a cell-mediated immune response; and a vaccine adjuvant comprising a thiosemicarbazone or derivative thereof, in an amount effective to potentiate the cell-mediated immune response to the vaccine.

[0110] Other embodiments of a method of adminstering a vaccine comprise separately administering a vaccine in an amount effective to stimulate a cell-mediated immune response; and a vaccine adjuvant comprising a thiosemicarbazone or derivative thereof, in an amount effective to potentiate the cell-mediated immune response to the vaccine, wherein the vaccine adjuvant is adminstered either prior to or subsequent to administration of the vaccine.

BRIEF DESCRIPTION OF THE DRAWINGS

[0111] Figure 1 shows candidate small molecule immuno-potentiators identified *in vitro* by measuring TNF-alpha production by human PBMC.

[0112] Figure 2 shows thiosemicarbazone cytokine induction at several concentrations.

[0113] Figure 3 depicts a high throughput assay for small molecule immune potentiator screen.

[0114] Figure 4 depicts dual functional HCV anti-virals and immune potentiators.

DETAILED DESCRIPTION OF THE INVENTION

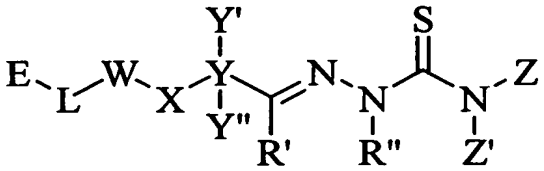
[0115] One embodiment of the invention is directed to a method of inducing an immunostimulatory effect in a patient comprising administering a thiosemicarbazone compound in an amount effective to stimulate a cell-mediated immune response.

[0116] One preferred embodiment of the method of inducing an immunostimulatory effect in a patient is directed to a vaccine adjuvant composition comprising a vaccine in an amount effective to stimulate a cell-mediated immune response and, as a vaccine adjuvant, a thiosemicarbazone or derivatives thereof, in an amount effective to potentiate the cell-mediated immune response to the vaccine.

[0117] As is well-understood in the art, a vaccine may be prophylactic and/or therapeutic in nature. The vaccines and vaccine compositions disclosed herein likewise may be used prophylactically or therapeutically.

[0118] When the thiosemicarbazone is administered as a vaccine adjuvant, it may be administered simultaneously with the vaccine, prior to the vaccine, and even after vaccine administration.

[0119] Preferably, the thiosemicarbazone is a compound of formula I, the tautomers thereof, and the pharmaceutically acceptable salts, esters, or prodrugs thereof:



I

[0120] E is absent or selected from the group consisting of alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, heteroaryl, and substituted heteroaryl;

[0121] L is absent or is selected from the group consisting of oxo, amino, alkylene, substituted alkylene, alkoxy, alkylamino, aminoalkyl, heterocyclyl, carbocyclyl, and arbonyl;

[0122] W is absent or selected from the group consisting of cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, heteroaryl, and substituted heteroaryl;

[0123] X is absent or is selected from the group consisting og oxo, amino, alkylene, substituted alkylene, alkoxy, alkylamino, aminoalkyl, heterocyclyl, carbocyclyl, and carbonyl;

[0124] Y is selected from the group consisting of cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heterocyclyl, substituted heterocyclyl, heteroaryl, and substituted heteroaryl;

[0125] Y' is absent or is selected from the group consisting of halo, nitro, alkyl, substituted alkyl, and optionally substituted heterocyclyl, amino, alkylamino, dialkylamino;

[0126] Y" is absent or is selected from the group consisting of halo, nitro, alkyl, substituted alkyl, and optionally substituted heterocyclyl, amino, alkylamino, dialkylamino;

[0127] R' is H, alkyl, or substituted alkyl;

[0128] R'' is H, or

[0129] R' and R'' are taken together to form a heterocyclic ring;

[0130] Z and Z' are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, aryl, substituted aryl, arylalkyl, substituted arylalkyl, heteroaryl, substituted heteroaryl, heteroarylalkyl, substituted heteroarylalkyl, alkoxy, substituted alkoxy, aminocarbonyl, alkoxycarbonyl, carboxyl sulfonyl, methanesulfonyl, and substituted or unsubstituted alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, heteroarylcarbonyloxy, heteroaralkylcarbonyloxy, alkylaminocarbonyloxy, arylamino-carbonyloxy, formyl, loweralkylcarbonyl, loweralkoxycarbonyl, aminocarbonyl, aminoaryl, alkylsulfonyl, sulfonamido, aminoalkoxy, alkylamino, heteroarylamino, alkylcarbonylamino, alkylaminocarbonylamino, arylaminocarbonylamino, aralkylcarbonylamino, heteroarylcarbonylamino, arylcarbonylamino, cycloamidino, cycloalkyl, cycloimido, arylsulfonyl and arylsulfonamido.

[0131] Alternatively, Z and Z' are taken together to form a heterocyclic group or substituted heterocyclic group.

[0132] The above method of inducing an immunostimulatory effect in a patient includes the administration of the thiosemicarbazone compound to enhance the efficacy of a therapeutic treatment by stimulating a local immune response in selected cells or tissues of the patient.

[0133] The above method of stimulating a local immune response in selected cells or tissues of a patient includes the stimulation of a local immune response wherein the selected cells or tissues are infected or cancerous. In one embodiment the selected cells or tissues are infected with a fungus or bacterium. In another embodiment the selected cells are infected with an allergen. In another embodiment the selected cells are infected with a virus. In still a more particular embodiment the virus is the as coronavirus, SARS-associated coronavirus (SARS-CoV), HCV, HIV, HBV, HSV, H. pylori, HSV Type 1 or 2, or Human Papilloma Virus.

[0134] The vaccine adjuvant compositions of the invention can contain further pharmaceutically acceptable ingredients, excipients, carriers, and the like well known to those skilled in the art.

[0135] The invention is also directed to administering the vaccine adjuvant composition. The vaccine is administered in an amount effective to stimulate an immune response. The amount that constitutes an effective amount depends, inter alia, on the particular vaccine used, the particular adjuvant compound being administered and the amount thereof, the immune response that is to be enhanced (humoral or cell mediated), the state of the immune system (e.g., suppressed, compromised, stimulated), and the desired therapeutic result. Accordingly it is not practical to set forth generally the amount that constitutes an effective amount of the vaccine. Those of ordinary skill in the art, however, can readily determine the appropriate amount with due consideration of such factors.

[0136] The vaccine adjuvant compositions of the invention can be administered to animals, e.g., mammals (human and non-human), fowl, and the like according to conventional methods well known to those skilled in the art (e.g., orally, subcutaneously, nasally, topically).

[0137] Suitable vaccines include, but are not limited to, any material that raises either humoral or cell mediated immune response, or both. Suitable vaccines include live viral and bacterial immunogens and inactivated viral, tumor-derived, protozoal, organism-derived, fungal, and bacterial immunogens, toxoids, toxins, polysaccharides, proteins, glycoproteins,

peptides, and the like. Conventional vaccines, such as those used in connection with BCG (live bacteria), cholera, plague, and typhoid (killed bacteria), hepatitis B, influenza, inactivated polio, and rabies (inactivated virus), measles, mumps, rubella, oral polio, and yellow fever (live virus), tetanus and diphtheria (toxoids), hemophilus influenzae b, meningococcal, and pneumococcal (bacterial polysaccharides) also can be used.

[0138] Furthermore, it is contemplated that certain currently experimental vaccines, especially materials such as recombinant proteins, glycoproteins, and peptides that do not raise a strong immune response, will also find use in connection with the thiosemicarbazone. Exemplary experimental subunit immunogens include those related to viral disease such as adenovirus, AIDS, chicken pox, cytomegalovirus, dengue, feline leukemia, fowl plague, hepatitis A, hepatitis B, hepatitis C, HSV-1, HSV-2, hog cholera, influenza A, influenza B, Japanese encephalitis, measles, parainfluenza, rabies, respiratory syncytial virus, rotavirus, wart, and yellow fever.

[0139] Specific antigens for use with the invention include, but are not limited to, those listed below. The number(s) in parenthesis indicate representative resources of the antigen. The resource list follows the antigen list and each resource is incorporated by reference in its entirety.

[0140] Specific antigens include: a protein antigen from N. meningitides serogroup B (1-7); an outer-membrane vesicle (OMV) preparation from N. meningitides serogroup B. (8, 9, 10, 11); a saccharide antigen from N. meningitides serogroup A, C W135 and/or Y, such as the oligosaccharide (12) from serogroup C (13); a saccharide antigen from Streptocaccus pneumoniae (14, 15, 16); an antigen from N. gonorrhoeae (1, 2, 3); an antigen from Chlamydia pneumoniae (17, 18, 19, 20, 21, 22, 23); an antigen from Chlamydia trachomatis (24); an antigen from hepatitis A virus, such as inactive virus (25, 26); an antigen from hepatitis B virus, such as the surface and/or core antigens [e.g. 26, 27]; an antigen from hepatitis C virus (28); an antigen from Bordetella pertussis, such as petussis holotoxin (PT) and filamentous haemagglutinin (FHA) from B. pertussis, optionally also combination with pertactin and/or agglutinogens 2 and 3 (29, 30); a diphtheria antigen, such as a diphtheria toxoid (31:chapter 3) e.g. the CRM197 mutant (32); a tetanus antigen, such as a tetanus toxioid (31:chapter 4); a protein antigen from Helicobacter pylori such as CagA (33), VacA (33), NAP (34), HopX (5), HopY (35) and/or urease; a saccharide antigen from Haemophilus influenzae B (13); an antigen from Porphyromonas gingivalis (36); polio antigen(s) (37, 38)

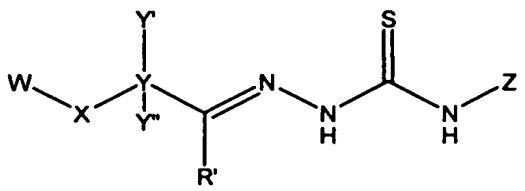
such as IPV or OPV; rabies antigen(s) (39) such lyophilized inactivated virus (40, RabAvert™); measles, mumps and/or rubella antigens (31: chapters 9, 10, & 11); influenza antigen(s) (31:chapter 19), such as the haemagglutinin and/or neuraminidase surface proteins; an antigen from Moraxella catarrhalis (41); an antigen from Streptococcus agalactiae (group B streptococcus) (42, 43); an antigen from Streptococcus pyogenes (group A streptococcus) (43, 44, 45); and an antigen from Staphylococcus aureus (46).

[0141] The composition may comprise one or more of the above antigens.

[0142] Where a saccharide or carbohydrate antigen is used, it is preferably conjugated to a carrier protein in order to enhance immunogenicity (47-6). Preferred carrier proteins are bacterial toxine or toxiods, such as diphtheria or tetanus toxoids. The CRM197 diphtheria toxoid is particularly preferred. Other suitable carrier proteins include the N. meningitides outer membrane protein (57), synthetic peptides (58, 59), heat shock proteins (60), pertussis proteins (61, 62), protein D from H. influenzae (63), toxin A or B from C. difficile (64) etc. Where a mixture comprises capsular saccharides from both serogroups A and C, it is preferred that the ratio (w/w) of MenA saccharide:MenC saccharide is greater than 1 (e.g. 2:1, 3:1, 4:4, 5:1, 10:1 or higher). Saccharides from different serogroups of N.meningitides may be conjugated to the same or different carrier proteins.

[0143] Any suitable conjugation reaction can be used, with any suitable liner where necessary. Toxic protein antigens may be detoxified where necessary (e.g. detoxification of pertussis toxin by chemical and/or genetic means (30)). Where a diphtheria antigen is included in the composition it is preferred also to include tetanus antigens and pertussis antigens. Similarly, where a tetanus antigen is included it is preferred also to include diphtheria and pertussis antigens. Similar, where pertussis antigen is included it is preferred also to include diphtheria and tetanus antigens.

[0144] In another embodiment, the invention provides a method of treating a viral infection in a mammal comprising administering to the mammal a compound of formula II or its salts, prodrugs, or tautomers thereof:



II

[0145] wherein:

[0146] W is an aryl, substituted aryl, heteroaryl or substituted heteroaryl group having one ring or two fused rings;

[0147] X is absent or is selected from the group consisting of oxo, amino, alkylene, substituted alkylene, alkoxy, alkylamino, aminoalkyl, heterocyclyl, and carbocyclyl. Preferably X is absent or is selected from the group consisting of piperizinyl, –O(CH_2)n-; -(CH_2)n-O-; -O-; -C(O)O-; -NH-(CH_2)$_m$-; -(CH_2)$_m$-NH-; -NH-(CH_2)m-NH-; -N(CH_2)n-(CH_2)$_m$-NH-; -N(CH_2)$_n$-(CH_2)$_m$-N(CH_2)$_p$-; -NH-(CH_2)$_m$-N(CH_2)$_n$ and –O-(CH_2)p-O-, wherein n, m, and p are 1 to 3. More preferably, X is absent or is selected from the group consisting of –CH_2-O-; -O-CH_2-; -CH_2; -O-; -C(O)O-; -NHCH_2-; -NHCH_2CH_2; and -OCH_2CH_2O-;

[0148] Y is an aryl, substituted aryl, heteroaryl, or substituted heteroaryl group having one ring or two fused rings. Preferably, Y is selected from the group consisting of phenyl, furanyl, pyrrolyl, pyrazolyl, pyrazinyl, thiazolyl, pyrimidinyl, and imidazolyl;

[0149] Alternatively, X does not exist and Y and W together form an arly, substituted aryl, heteroaryl, or substituted heteroaryl group having at least two fused rings. Preferably, Y and W together form an unsubstituted or substituted nitrogen-containing fused heteroaryl group having at least two fused rings. More preferably an unsubstituted or substituted quinolinyl, indolyl, benzo[g]indolyl, benzindolyl, or benzofuranyl.

[0150] Y' is absent or is selected from the group consisting of halo, nitro, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, amino, alkylamino, and dialkylamino. Preferably, Y' is absent or is selected from the group consisting of halo; –CH_3; -OCH_3; -N(CH_2CH_3)$_2$; -phenyl; -Br; and -NO_2.

[0151] Y" is absent or is selected from the group consisting of halo, nitro, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, amino, alkylamino, and dialkylamino.

[0152] R' is H or CH_3;

[0153] Z is selected from the group consisting of hydrogen, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, heterocyclylalkyl, and substituted heterocyclylalkyl. In one embodiment, Z is preferably hydrogen. In another embodiment, if Y is furanyl, then Z is selected from the group consisting of pyridylalkylene, piperidinylalkylene, morpholinylalkylene, and piperizinylalkylene.

[0154] In one embodiment, W is phenyl or phenyl substituted with at least one member selected from the group consisting of halogen; nitro; alkylamino; dialkylamino; alkyl; trifluoroalkyl; and trifluoroalkylalkoxy, preferably with at least one member selected from the group consisting of -Cl; -F; -Br; $-CF_3$; $-OCH_3$; $-NO_2$; CH_3; $-N(CH_3)_2$; and $-OCF_3$.

[0155] In another embodiment, W is a heteroaryl or substituted heteroaryl selected from the group consisting of furanyl, pyridinyl, pyrrolyl, pyrazolyl, pyrazinyl, thiazolyl, and imidazolyl, preferably pyridinyl. If substituted, the heteroaryl is preferably substituted with at least one member selected from the group consisting of halogen; nitro; alkylamino; dialkylamino; alkyl; trifluoroalkyl; and trifluoroalkylalkoxy, more preferably at least one member selected from the group consisting of -Cl; -F; -Br; $-CF_3$; $-OCH_3$; $-NO_2$; CH_3; $-N(CH_3)_2$; and $-OCF_3$.

[0156] In one embodiment, if Y is pyrrol, the Y' and Y" are alkyl. In another embodiment, if Y is phenyl, and Y' is alkoxy, then Y" is a halogen. In another embodiment if Y is pyrazolyl, then Y' is aryl. In another embodiment, if Y is aryl with two fused rings, then Y' is alkoxy and Y" is alkyl.

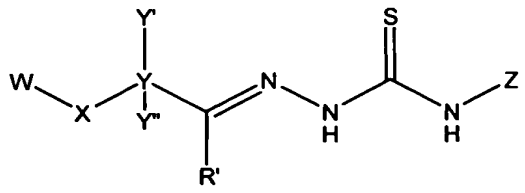
[0157] In one preferred embodiment, Y is pyrrol and Y' and Y" are each $-CH_3$, X is absent, and W is phenyl substituted with nitro, dimethylamine, Cl, F, or CH_3.

[0158] In other preferred embodiments, Z is hydrogen, Y is furanyl, Y' does not exist, X is absent, and W is phenyl substituted with Cl or CF_3; or Z is hydrogen, Y is phenyl, Y' is $-OCH_3$, X is $-OCH_2-$ and W is phenyl substituted with one or two Cl; or Z is hydrogen, Y is phenyl, Y' is nitro, X is $-NHCH_2-$ and W is phenyl substituted with Cl.

[0159] In another embodiment, the invention provides a method of treating a patient with an HCV infection by administering to the patient a compound of formula II, or its salts, prodrugs, or tautomers thereof as described above.

[0160] The patient is preferably a mammal, and in some embodiments, a human. The compounds may be injected or taken orally.

[0161] In another embodiment, the invention provides a method of treating a patient with an HCV infection by administering to the patient a compound of formula II, or its salts, prodrugs, or tautomers thereof.



II

[0162] R' is H or $-CH_3$.

[0163] W is an aryl, substituted aryl, heteroaryl, or substituted heteroaryl group having one ring or two fused rings. Preferably, W is phenyl or phenyl substituted with at least one member selected from the group consisting of halogen; nitro; alkylamino; dialkylamino; alkyl; trifluoroalkyl; and trifluoroalkylalkoxy, preferably with at least one member selected from the group consisting of -Cl; -F; -Br; $-CF_3$; $-OCH_3$; $-NO_2$; CH_3; $-N(CH_3)_2$; and $-OCF_3$.

[0164] X is absent or is selected from the group consisting of oxo, amino, alkylene, substituted alkylene, alkoxy, alkylamino, aminoalkyl, heterocyclyl, and carbocyclyl.

[0165] Y is an aryl or heteroaryl group having one ring or two fused rings.

[0166] Alternatively, X does not exist and Y and W together form an aryl, substituted aryl, heteroaryl, or substituted heteroaryl group having at least two fused rings.

[0167] Y' is absent or is selected from the group consisting of nitro, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, amino, alkylamino, and dialkylamino;

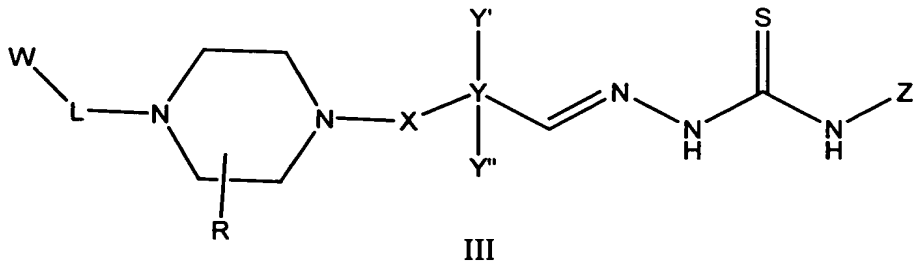
[0168] Y" is absent or is selected from the group consisting of nitro, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, amino, alkylamino, and dialkylamino;

[0169] Z is selected from the group consisting of hydrogen, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, heterocyclylalkyl, and substituted heterocyclylalkyl.

[0170] The patient is preferably a mammal, and in some embodiments, a human. The compounds may be injected or taken orally.

[0171] The invention is also directed to novel compounds as defined below by formulas III-VII, and salts, prodrugs, or tautomers thereof, as well as pharmaceutical compositions containing the compounds and methods of treating or preventing viral infections, in particular HCV, by administering such compounds to a mammal in need thereof.

[0172] The invention is also directed to novel compounds defined by formula III and salts, prodrugs, or tautomers thereof:



III

[0173] W is an aryl, substituted aryl, heteroaryl, or substituted heteroaryl group. Preferably W is phenyl or substituted phenyl. If substituted, phenyl is preferably substituted with at least one member selected from the group consisting of Br, Cl, F, and CF_3.

[0174] L and X are each independently absent or independently selected from the group consisting of lower alkyl and carbonyl;

[0175] R is absent or selected from the group consisting of carbonyl, amino, alkyl, substituted alkyl, alkylamino, and dialkylamino.

[0176] Y is an aryl or heteroaryl group. Y is preferably selected from the group consisting of phenyl, furanyl, pyrridinyl, pyrrolyl, pyrazolyl, pyrazinyl, thiazolyl, pyrimidinyl, and imidazolyl. More preferably, Y is phenyl, furanyl, or pyrimidinyl.

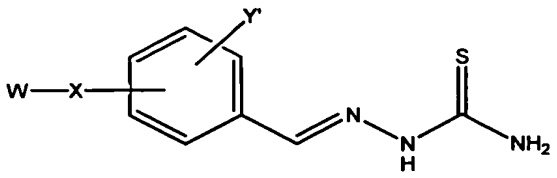
[0177] Y' is absent or selected from the group consisting of halo, alkyl, substituted alkyl, heterocyclyl, amino, alkylamino, dialkylamino, and nitro. If present, Y' is preferably fluro, nitro or piperizinyl.

[0178] Y" is absent or selected from the group consisting of halo, alkyl, substituted alkyl, heterocyclyl, amino, alkylamino, dialkylamino, and nitro. If present, Y' is preferably fluoro, nitro or piperizinyl.

[0179] Z is hydrogen, or if Y is furanyl, then Z may be selected from the group consisting of alkyl, substituted alkyl, heterocyclyl, amino, alkylamino, dialkylamino, and nitro.

[0180] In a preferred embodiment, W is phenyl or phenyl substituted with $-CF_3$ or Cl; Y is phenyl; Y' is nitro; and Z is H.

[0181] The present invention is also directed to novel compounds defined by formula IV and salts, prodrugs, or tautomers thereof:



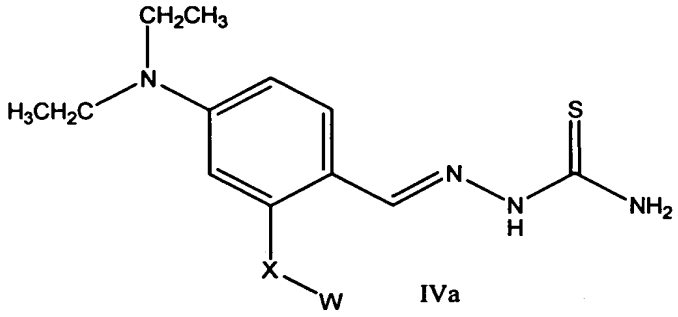
IV

[0182] W is a phenyl, substituted phenyl, pyridinyl, or substituted pyridinyl group. W is preferably substituted with at least one member selected from the group consisting of -Cl; -F; -Br; $-CF_3$; $-OCH_3$; $-NO_2$; $-CH_3$; $-N(CH_3)_2$; and $-OCF_3$.

[0183] X is alkoxy or alkylamino.

[0184] Y' is dialkylamino,fluro, or nitro.

[0185] In one embodiment, the compound IV is defined as IVa and salts, prodrugs, or tautomers thereof:

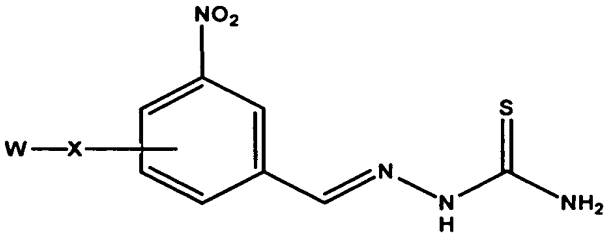


IVa

[0186] X is alkoxy, preferably $-OCH_2-$.

[0187] W is phenyl substituted with at least one member selected from the group consisting of -Cl; -F; -Br; $-CF_3$; $-OCH_3$; $-NO_2$; $-CH_3$; $-N(CH_3)_2$; and $-OCF_3$.

[0188] In one embodiment, the compound IV is defined as IVb and salts, prodrugs, or tautomers thereof:

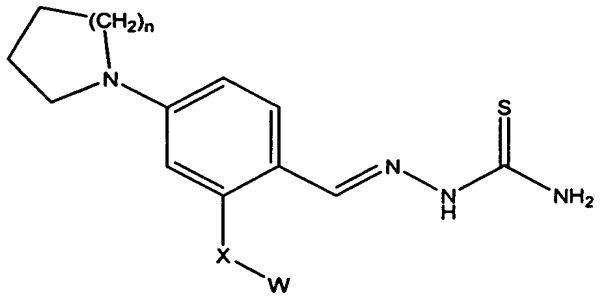


IVb

[0189] X is alkylamino, preferably $-NHCH_2CH_2-$ or $-NHCH_2-$.

[0190] W is pyridinyl or phenyl substituted with at least one member selected from the group consisting of Cl, F, and CF_3, preferably pyridinyl or phenyl substituted with Cl, F, and CF_3.

[0191] In one embodiment, the compound IV is defined as IVc and salts, prodrugs, or tautomers thereof:



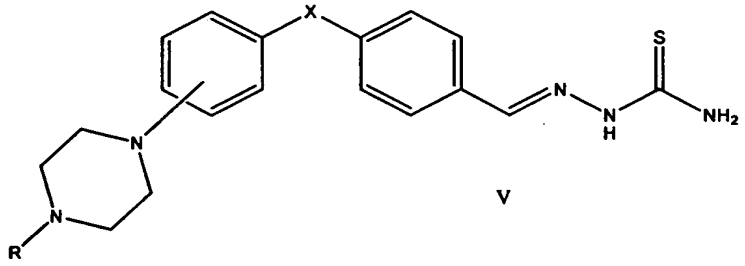
IVc

[0192] X is alkoxy, preferably $-OCH_2-$.

[0193] W is phenyl substituted with at least one member selected from the group consisting of -Cl; -F; -Br; $-CF_3$; $-OCH_3$; $-NO_2$; $-CH_3$; $-N(CH_3)_2$; and $-OCF_3$.

n is an integer from 1 and 3.

[0194] The invention is also directed to novel compounds defined by formula V and salts, prodrugs, or tautomers thereof

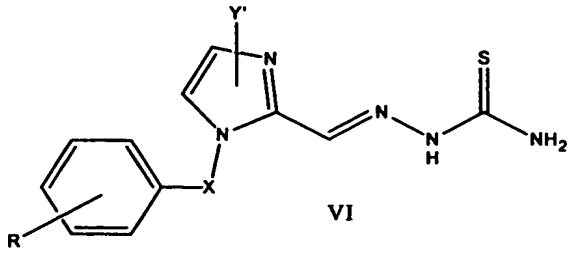


V

[0195] R is an alkyl group, preferably methyl.

[0196] X is alkoxy, preferably $-OCH_2-$; $-OCH_2CH_2-$; $-CH_2O-$; or $-CH_2CH_2O-$.

[0197] The invention is also directed to novel compounds defined by formula VI and salts, prodrugs, or tautomers thereof:



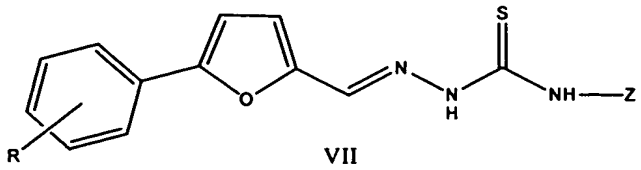
VI

[0198] X is absent or an alkylene, preferably $-CH_2CH_2-$.

[0199] Y' is absent or is an alkyl group, preferably Y' is absent or is methyl.

[0200] R is a halogen, preferably Cl.

[0201] The invention is also directed to novel compounds defined by formula VII and salts, prodrugs, or tautomers thereof:

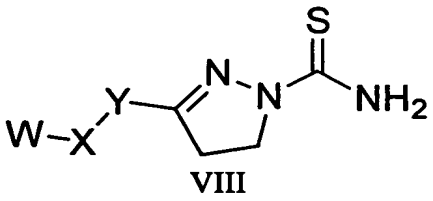


VII

[0202] R is nitro and Z is H; or R is Cl and Z is selected from the group consisting of alkyl, pyridylalkylene, piperidinylalkylene, morpholinylalkylene, and piperizinylalkylene, preferably methyl, pyridylmethylene, piperidinylethylene, morpholinylethylene, piperizinylmethylene, piperizinylethylene, and morpholinylbutylene.

[0203] The invention is also directed to a vaccine adjuvant composition comprising a vaccine in an amount effective to stimulate a cell-mediated immune response and, as a vaccine adjuvant, a a compound of formulas II through VI or derivatives thereof, in an amount effective to potentiate the cell-mediated immune response to the vaccine.

[0204] The invention is also directed to novel compounds defined by formula VIII and salts, prodrugs, or tautomers thereof:



VIII

[0205] wherein:

[0206] Y is an aryl or heteroaryl group. Y is preferably selected from the group consisting of phenyl, furanyl, pyrridinyl, pyrrolyl, pyrazolyl, pyrazinyl, thiazolyl, and imidazolyl. More preferably, Y is furanyl.

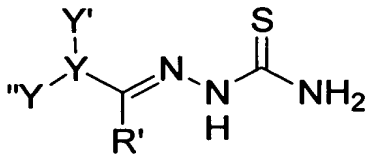
[0207] X is absent or is selected from the group consisting of oxo, amino, alkylene, and substituted alkylene. More preferably, X is absent.

[0208] W is a phenyl, substituted phenyl, pyridinyl, or substituted pyridinyl group. W is preferably substituted with at least one member selected from the group consisting of -Cl; -F; -Br; $-CF_3$; $-OCH_3$; $-NO_2$; $-CH_3$; $-N(CH_3)_2$; and $-OCF_3$.

[0209] The invention is also directed to a pharmaceutical composition comprising a therapeutically effective amount of a compound of formulas III through VIII a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer and a pharmaceutically suitable carrier or excipient.

[0210] The invention also provides a method of treating viral infections, including HCV, in a subject comprising administering to the subject a compound of formulas III though VIII, a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer.

[0211] The invention also provides a method of treating an HCV infection, in a subject comprising administering to the subject a compound of the following formula (IX), a tautomer of the compound, a pharmaceutically acceptable salt of the compound, or a pharmaceutically acceptable salt of the tautomer.



IX

[0212] wherein;

[0213] R' is H or lower alkyl.

[0214] Y is an aryl or heteroaryl group having one ring or two fused rings. Preferably, Y is selected from the group consisting of phenyl, furanyl, pyrrolyl, pyrazolyl, pyrazinyl, thiazolyl, pyrimidinyl, and imidazolyl.

[0215] Y' is selected from the group consisting of nitro, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, heterocyclyl, substituted heterocyclyl, amino, alkylamino, and dialkylamino.

[0216] Y" is absent or is selected from the group consisting of halo, nitro, alkyl, substituted alkyl, heterocyclyl, substituted heterocyclyl, amino, alkylamino, and dialkylamino.

[0217] DEFINITIONS:

[0218] As used above and elsewhere herein the following terms and abbreviations have the meanings defined below:

[0219]	AcOH	Acetic Acid
[0220]	ATP:	Adenosine triphosphate
[0221]	BCG	Mycobacterium bovis bacillus Calmette-Guerin
[0222]	BOC	tert-butoxycarbonyl
[0223]	BSA:	Bovine Serum Albumin
[0224]	DIBAL-H	diisobutylaluminum hydride
[0225]	DCM	dichloromethane
[0226]	DIEA	diisopropylethylamine
[0227]	DMA:	N,N-Dimethylacetamide
[0228]	DMF:	N,N-Dimethylformamide
[0229]	DMSO	dimethyl sulfoxide
[0230]	dppf:	1,1'(diphenylphosphino)ferrocene
[0231]	DTT:	DL-Dithiothreitol
[0232]	EDTA:	Ethylene diamine tetraacetic acid
[0233]	EtOAc:	Ethyl acetate
[0234]	EtOH:	Ethanol
[0235]	FHA	Filamentous haemaglutinin
[0236]	GCMS	Gas Chromatography / Mass Spectroscopy
[0237]	H. Pylori	Helicobacter Pylori
[0238]	HAV	Hepatitis A Virus
[0239]	HBTU:	O-Benzotriazol-1-yl-N,N,N',N'-tetramethyluronium hexafluorophosphate
[0240]	HBV	Hepatitis B Virus
[0241]	HCV	Hepatitis C Virus
[0242]	HIV	Human Immunodeficiency Virus
[0243]	HPLC	High Performance Liquid Chromatography
[0244]	HSV	Herpes Simplex Virus
[0245]	IC50 value:	The concentration of an inhibitor that causes a 50 % reduction in a measured activity.
[0246]	IFN	Interferon

[0247]	IL	Interleukin
[0248]	IMS	Immunomagnetic separation
[0249]	IPV	Inactivated polio virus
[0250]	LCMS	Liquid Chromatography / Mass Spectroscopy
[0251]	LPS	Lipopolysaccharide
[0252]	Men A	Type A meningitis
[0253]	Men C	Type C meningitis
[0254]	MeOH:	Methanol
[0255]	NANB	Non-A, non-B hepatitis
[0256]	NMP:	N-methylpyrrolidone
[0257]	NMR	Nuclear magnetic resonance
[0258]	OMV	Outer membrane vesicle
[0259]	PBMC	Peripheral blood mononuclear cells
[0260]	PT	Petussis holotoxin
[0261]	Rt	Room temperature (25°C)
[0262]	SARS	Severe Acute Respiratory Syndrome
[0263]	SMIP	Small Molecule Immune Potentiator
[0264]	THF:	Tetrahydrofuran
[0265]	TLC	Thin-layer chromatography
[0266]	TNF-alpha	Tumour necrosis factor-a

[0267]

[0268] Generally, reference to a certain element such as hydrogen or H is meant to include all isotopes of that element. For example, if an R group is defined to include hydrogen or H, it also includes deuterium and tritium.

[0269] The term "absent" in reference to a particular substituent means the substuent is not present or, when between two other moieties, the "absent" substituent is a covalent bond therebetween.

[0270] The phrase "alkyl" refers to alkyl groups that do not contain heteroatoms. Thus the phrase includes straight chain alkyl groups such as methyl, ethyl, propyl, butyl, pentyl, hexyl, heptyl, octyl, nonyl, decyl, undecyl, dodecyl and the like. The phrase also includes branched chain isomers of straight chain alkyl groups, including but not limited to, the following which are provided by way of example: $-CH(CH_3)_2$,

$-CH(CH_3)(CH_2CH_3)$, $-CH(CH_2CH_3)_2$, $-C(CH_3)_3$, $-C(CH_2CH_3)_3$, $-CH_2CH(CH_3)_2$, $-CH_2CH(CH_3)(CH_2CH_3)$, $-CH_2CH(CH_2CH_3)_2$, $-CH_2C(CH_3)_3$, $-CH_2C(CH_2CH_3)_3$, $-CH(CH_3)CH(CH_3)(CH_2CH_3)$, $-CH_2CH_2CH(CH_3)_2$, $-CH_2CH_2CH(CH_3)(CH_2CH_3)$, $-CH_2CH_2CH(CH_2CH_3)_2$, $-CH_2CH_2C(CH_3)_3$, $-CH_2CH_2C(CH_2CH_3)_3$, $-CH(CH_3)CH_2CH(CH_3)_2$, $-CH(CH_3)CH(CH_3)CH(CH_3)_2$, $-CH(CH_2CH_3)CH(CH_3)CH(CH_3)(CH_2CH_3)$, and others. The phrase also includes cyclic alkyl groups such as cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl, and cyclooctyl and such rings substituted with straight and branched chain alkyl groups as defined above. Thus alkyl groups include primary alkyl groups, secondary alkyl groups, and tertiary alkyl groups. Preferred alkyl groups include straight and branched chain alkyl groups and cyclic alkyl groups having 1 to 12 carbon atoms.

[0271] The phrase "loweralkyl" refers to an acyclic alkyl group as described above. "Lower" is about 1 to about 8 carbon atoms, preferably about 1 to about 6 carbon atoms.

[0272] The phrase "substituted alkyl" refers to an alkyl group as defined above in which one or more bonds to a carbon(s) or hydrogen(s) are replaced by a bond to non-hydrogen and non-carbon atoms such as, but not limited to, a halogen atom such as F, Cl, Br, and I; an oxygen atom in groups such as hydroxyl groups, alkoxy groups, aryloxy groups, and ester groups; a sulfur atom in groups such as thiol groups, alkyl and aryl sulfide groups, sulfone groups, sulfonyl groups, and sulfoxide groups; a nitrogen atom in groups such as amines, amides, alkylamines, dialkylamines, arylamines, alkylarylamines, diarylamines, N-oxides, imides, and enamines; a silicon atom in groups such as in trialkylsilyl groups, dialkylarylsilyl groups, alkyldiarylsilyl groups, and triarylsilyl groups; and other heteroatoms in various other groups. Substituted alkyl groups also include groups in which one or more bonds to a carbon(s) or hydrogen(s) atom is replaced by a higher-order bond (e.g., a double- or triple-bond) to a heteroatom such as oxygen in oxo, carbonyl, carboxyl, and ester groups; nitrogen in groups such as imines, oximes, hydrazones, and nitriles. Substituted alkyl groups further include alkyl groups in which one or more bonds to a carbon(s) or hydrogen(s) atoms is replaced by a bond to an aryl, heterocyclyl group, or cycloalkyl group. Preferred substituted alkyl groups include, among others, alkyl groups in which one or more bonds to a carbon or hydrogen atom is/are replaced by one or more bonds to fluorine atoms. Another preferred substituted alkyl group is the trifluoromethyl group and other alkyl groups that contain the trifluoromethyl group. Other preferred substituted alkyl groups include those in which one or more bonds to a carbon or hydrogen atom is replaced by a bond to an oxygen

atom such that the substituted alkyl group contains a hydroxyl, alkoxy, or aryloxy group. Still other preferred substituted alkyl groups include alkyl groups that have an amine, or a substituted or unsubstituted alkylamine, dialkylamine, arylamine, (alkyl)(aryl)amine, diarylamine, heterocyclylamine, diheterocyclylamine, (alkyl)(heterocyclyl)amine, or (aryl)(heterocyclyl)amine group.

[0273] The phrase "alkenyl" refers to straight and branched chain and cyclic groups such as those described with respect to alkyl groups as defined above, except that at least one double bond exists between two carbon atoms. Examples include, but are not limited to vinyl, $-CH=C(H)(CH_3)$, $-CH=C(CH_3)_2$, $-C(CH_3)=C(H)_2$, $-C(CH_3)=C(H)(CH_3)$, $-C(CH_2CH_3)=CH_2$, cyclohexenyl, cyclopentenyl, cyclohexadienyl, butadienyl, pentadienyl, and hexadienyl among others. The phrase "substituted alkenyl" has the same meaning with respect to alkenyl groups that substituted alkyl groups had with respect to unsubstituted alkyl groups. A substituted alkenyl group includes alkenyl groups in which a non-carbon or non-hydrogen atom is bonded to a carbon double bonded to another carbon and those in which one of the non-carbon or non-hydrogen atoms is bonded to a carbon not involved in a double bond to another carbon.

[0274] The phrase "alkynyl" refers to straight and branched chain groups such as those described with respect to alkyl groups as defined above, except that at least one triple bond exists between two carbon atoms. Examples include, but are not limited to $-C\equiv C(H)$, $-C\equiv C(CH_3)$, $-C\equiv C(CH_2CH_3)$, $-C(H_2)C\equiv C(H)$, $-C(H)_2C\equiv C(CH_3)$, and $-C(H)_2C\equiv C(CH_2CH_3)$ among others. The phrase "substituted alkynyl" has the same meaning with respect to alkynyl groups that substituted alkyl groups had with respect to unsubstituted alkyl groups. A substituted alkynyl group includes alkynyl groups in which a non-carbon or non-hydrogen atom is bonded to a carbon triple bonded to another carbon and those in which a non-carbon or non-hydrogen atom is bonded to a carbon not involved in a triple bond to another carbon.

[0275] The phrase "heterocyclyl" refers to both aromatic and nonaromatic ring compounds including monocyclic, bicyclic, and polycyclic ring compounds such as, but not limited to, quinuclidinyl, containing 3 or more ring members of which one or more is a heteroatom such as, but not limited to, N, O, and S. Although the phrase "unsubstituted heterocyclyl" includes condensed heterocyclic rings such as benzimidazolyl, it does not include heterocyclyl groups that have other groups such as alkyl or halo groups bonded to one of the ring members as compounds such as 2-methylbenzimidazolyl are substituted

heterocyclyl groups. Examples of heterocyclyl groups include, but are not limited to: unsaturated 3 to 8 membered rings containing 1 to 4 nitrogen atoms such as, but not limited to pyrrolyl, pyrrolinyl, imidazolyl, pyrazolyl, pyridyl, dihydropyridyl, pyrimidyl, pyrazinyl, pyridazinyl, triazolyl (e.g. 4H-1,2,4-triazolyl, 1H-1,2,3-triazolyl, 2H-1,2,3-triazolyl etc.), tetrazolyl, (e.g. 1H-tetrazolyl, 2H tetrazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 4 nitrogen atoms such as, but not limited to, pyrrolidinyl, imidazolidinyl, piperidinyl, piperazinyl; condensed unsaturated heterocyclic groups containing 1 to 4 nitrogen atoms such as, but not limited to, indolyl, isoindolyl, indolinyl, indolizinyl, benzimidazolyl, quinolyl, isoquinolyl, indazolyl, benzotriazolyl; unsaturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms such as, but not limited to, oxazolyl, isoxazolyl, oxadiazolyl (e.g. 1,2,4-oxadiazolyl, 1,3,4-oxadiazolyl, 1,2,5-oxadiazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms such as, but not limited to, morpholinyl; unsaturated condensed heterocyclic groups containing 1 to 2 oxygen atoms and 1 to 3 nitrogen atoms, for example, benzoxazolyl, benzoxadiazolyl, benzoxazinyl (e.g. 2H-1,4-benzoxazinyl etc.); unsaturated 3 to 8 membered rings containing 1 to 3 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, thiazolyl, isothiazolyl, thiadiazolyl (e.g. 1,2,3-thiadiazolyl, 1,2,4-thiadiazolyl, 1,3,4-thiadiazolyl, 1,2,5-thiadiazolyl, etc.); saturated 3 to 8 membered rings containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, thiazolodinyl; saturated and unsaturated 3 to 8 membered rings containing 1 to 2 sulfur atoms such as, but not limited to, thienyl, dihydrodithiinyl, dihydrodithionyl, tetrahydrothiophene, tetrahydrothiopyran; unsaturated condensed heterocyclic rings containing 1 to 2 sulfur atoms and 1 to 3 nitrogen atoms such as, but not limited to, benzothiazolyl, benzothiadiazolyl, benzothiazinyl (e.g. 2H-1,4-benzothiazinyl, etc.), dihydrobenzothiazinyl (e.g. 2H-3,4-dihydrobenzothiazinyl, etc.), unsaturated 3 to 8 membered rings containing oxygen atoms such as, but not limited to furyl; unsaturated condensed heterocyclic rings containing 1 to 2 oxygen atoms such as benzodioxolyl (e.g. 1,3-benzodioxoyl, etc.); unsaturated 3 to 8 membered rings containing an oxygen atom and 1 to 2 sulfur atoms such as, but not limited to, dihydrooxathiinyl; saturated 3 to 8 membered rings containing 1 to 2 oxygen atoms and 1 to 2 sulfur atoms such as 1,4-oxathiane; unsaturated condensed rings containing 1 to 2 sulfur atoms such as benzothienyl, benzodithiinyl; and unsaturated condensed heterocyclic rings containing an oxygen atom and 1 to 2 oxygen atoms such as benzoxathiinyl. Heterocyclyl groups also include those

described above in which one or more S atoms in the ring is double-bonded to one or two oxygen atoms (sulfoxides and sulfones). For example, heterocyclyl groups include tetrahydrothiophene, tetrahydrothiophene oxide, and tetrahydrothiophene 1,1-dioxide. Preferred heterocyclyl groups contain 5 or 6 ring members. More preferred heterocyclyl groups include morpholine, piperazine, piperidine, pyrrolidine, imidazole, pyrazole, 1,2,3-triazole, 1,2,4-triazole, tetrazole, thiomorpholine, thiomorpholine in which the S atom of the thiomorpholine is bonded to one or more O atoms, pyrrole, homopiperazine, oxazolidin-2-one, pyrrolidin-2-one, oxazole, quinuclidine, thiazole, isoxazole, furan, and tetrahydrofuran.

[0276] The phrase "substituted heterocyclyl" refers to a heterocyclyl group as defined above in which one of the ring members is bonded to a non-hydrogen atom such as described above with respect to substituted alkyl groups and substituted aryl groups. Examples, include, but are not limited to, 2-methylbenzimidazolyl, 5-methylbenzimidazolyl, 5-chlorobenzthiazolyl, 1-methyl piperazinyl, and 2-chloropyridyl among others.

[0277] The phrase "aryl" refers to aryl groups that do not contain heteroatoms. Thus the phrase includes, but is not limited to, groups such as phenyl, biphenyl, anthracenyl, naphthenyl by way of example. Although the phrase "aryl" includes groups containing condensed rings such as naphthalene, it does not include aryl groups that have other groups such as alkyl or halo groups bonded to one of the ring members, as aryl groups such as tolyl are considered herein to be substituted aryl groups as described below. A preferred unsubstituted aryl group is phenyl. Unsubstituted aryl groups may be bonded to one or more carbon atom(s), oxygen atom(s), nitrogen atom(s), and/or sulfur atom(s) in the parent compound, however.

[0278] The phrase "substituted aryl group" has the same meaning with respect to unsubstituted aryl groups that substituted alkyl groups had with respect to unsubstituted alkyl groups. However, a substituted aryl group also includes aryl groups in which one of the aromatic carbons is bonded to one of the non-carbon or non-hydrogen atoms described above and also includes aryl groups in which one or more aromatic carbons of the aryl group is bonded to a substituted and/or unsubstituted alkyl, alkenyl, or alkynyl group as defined herein. This includes bonding arrangements in which two carbon atoms of an aryl group are bonded to two atoms of an alkyl, alkenyl, or alkynyl group to define a fused ring system (e.g. dihydronaphthyl or tetrahydronaphthyl). Thus, the phrase "substituted aryl" includes, but is not limited to tolyl, 1,3-dichlorobenzene, and hydroxyphenyl among others.

[0279] The term "heteroaryl", as used herein, refers to a cyclic or bicyclic aromatic radical having from five to ten ring atoms in each ring of which one atom of the cyclic or bicyclic ring is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon, the radical being joined to the rest of the molecule via any of the ring atoms, such as, for example, pyridyl, pyrazinyl, pyrimidinyl, pyrrolyl, pyrazolyl, imidazolyl, thiazolyl, oxazolyl, isooxazolyl, thiadiazolyl, oxadiazolyl, thiophenyl, furanyl, quinolinyl, isoquinolinyl, and naphthyridinyl, and the like.

[0280] The term "substituted heteroaryl" as used herein refers to a heteroaryl group as defined herein substituted by independent replacement of one, two or three of the hydrogen atoms thereon with Cl, Br, F, I, OH, CN, C_1-C_3-alkyl, C_1-C_6-alkoxy, C_1-C_6-alkoxy substituted with aryl, haloalkyl, thioalkoxy, amino, alkylamino, dialkylamino, mercapto, nitro, carboxaldehyde, carboxy, alkoxycarbonyl and carboxamide. In addition, any one substituent may be an aryl, heteroaryl, or heterocycloalkyl group.

[0281] The term "biaryl" refers to a group or substituent to which two aryl groups, which are not condensed to each other, are bound. Exemplary biaryl compounds include, for example, phenylbenzene, diphenyldiazene, 4-methylthio-1-phenylbenzene, phenoxybenzene, (2-phenylethynyl)benzene, diphenyl ketone, (4-phenylbuta-1,3-diynyl)benzene, phenylbenzylamine, (phenylmethoxy)benzene, and the like. Preferred unsubstituted or substituted biaryl groups include: 2-(phenylamino)-N-[4-(2-phenylethynyl)phenyl]acetamide, 1,4-diphenylbenzene, 2,4-dichloro-1-(2-methylphenyl)benzene, N-[4-(2-phenylethynyl)phenyl]-2-[benzylamino]acetamide, and [4-(2-phenylethynyl)phenyl]pyrrole.

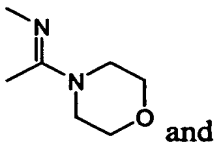
[0282] The term "heteroarylaryl" refers to a biaryl group where one of the aryl groups is a heteroaryl group. Exemplary heteroarylaryl groups include, for example, 2-phenylpyridine, phenylpyrrole, 3-(2-phenylethynyl)pyridine, phenylpyrazole, 5-(2-phenylethynyl)-1,3-dihydropyrimidine-2,4-dione, 4-phenyl-1,2,3-thiadiazole, 2-(2-phenylethynyl)pyrazine, 2-phenylthiophene, phenylimidazole, 3-(2-piperazinylphenyl)furan, 3-(2,4-dichlorophenyl)-4-methylpyrrole, and the like. Preferred unsubstituted or substituted heteroarylaryl groups include: 4-(2,4-dichlorophenyl)-3-methylpyrazole, 5-(2-phenylethynyl)pyrimidine-2-ylamine, 1-methoxy-4-(2-thienyl)benzene, 2-(3-nitrophenyl)thiophene, (tert-butoxy)-N-[(5-phenyl(3-pyridyl))methyl]carboxamide, hydroxy-N-[(5-phenyl(3-pyridyl))methyl]-amide, 2-(phenylmethylthio)pyridine, and benzylimidazole.

[0283] The term "heteroarylheteroaryl" refers to a biaryl group where both of the aryl groups are heteroaryl groups. Exemplary heteroarylheteroaryl groups include, for example, 3-pyridylimidazole, 2-imidazolylpyrazine, and the like. Preferred unsubstituted or substituted heteroarylheteroaryl groups include: 2-(4-piperazinyl-3-pyridyl)furan, diethyl(3-pyrazin-2-yl(4-pyridyl))amine, and dimethyl{2-[2-(5-methylpyrazin-2-yl)ethynyl](4-pyridyl)}amine.

[0284] "Optionally substituted" refers to the optional replacement of hydrogen with one or more monovalent or divalent radicals. Suitable substitution groups include, for example, hydroxyl, nitro, amino, imino, cyano, halo, thio, thioamido, amidino, imidino, oxo, oxamidino, methoxamidino, imidino, guanidino, sulfonamido, carboxyl, formyl, alkyl, substituted alkyl, halologweralkyl, loweralkoxy, halologweralkoxy, loweralkoxyalkyl, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, alkylthio, aminoalkyl, cyanoalkyl, benzyl, pyridyl, pyrazolyl, pyrrole, thiophene, imidazolyl, and the like.

[0285] "Substituted" refers to the definite replacement of hydrogen with one or more monovalent or divalent radicals. Suitable substitution groups include, for example, hydroxyl, nitro, amino, imino, cyano, halo, thio, thioamido, amidino, imidino, oxo, oxamidino, methoxamidino, imidino, guanidino, sulfonamido, carboxyl, formyl, alkyl, substituted alkyl, halologweralkyl, loweralkoxy, halologweralkoxy, loweralkoxyalkyl, alkylcarbonyl, arylcarbonyl, aralkylcarbonyl, heteroarylcarbonyl, heteroaralkylcarbonyl, alkylthio, aminoalkyl, cyanoalkyl, benzyl, pyridyl, pyrazolyl, pyrrole, thiophene, imidazolyl, and the like.

[0286] Representative substituted amidino and heterocycloamidino groups include, for example, those shown below. These amidino and heterocycloamidino groups can be further substituted as will be apparent to those having skill in the organic and medicinal chemistry arts in conjunction with the disclosure herein.



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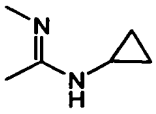
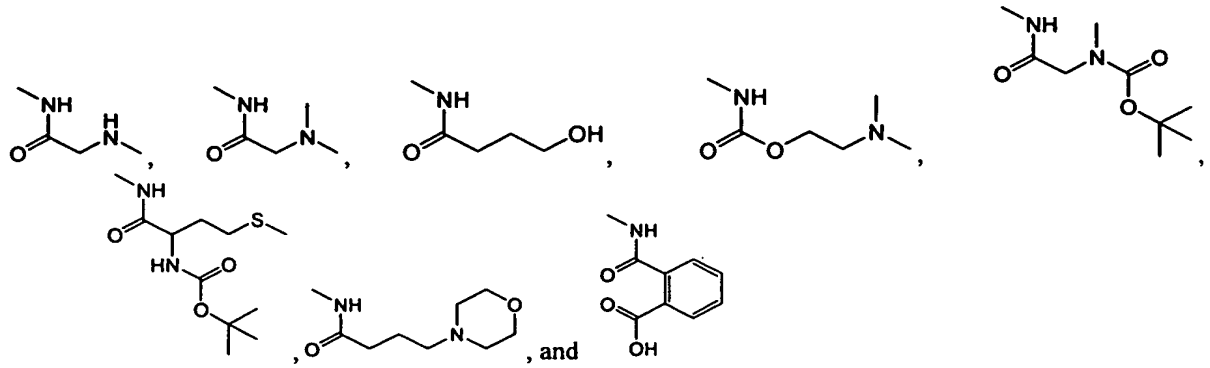
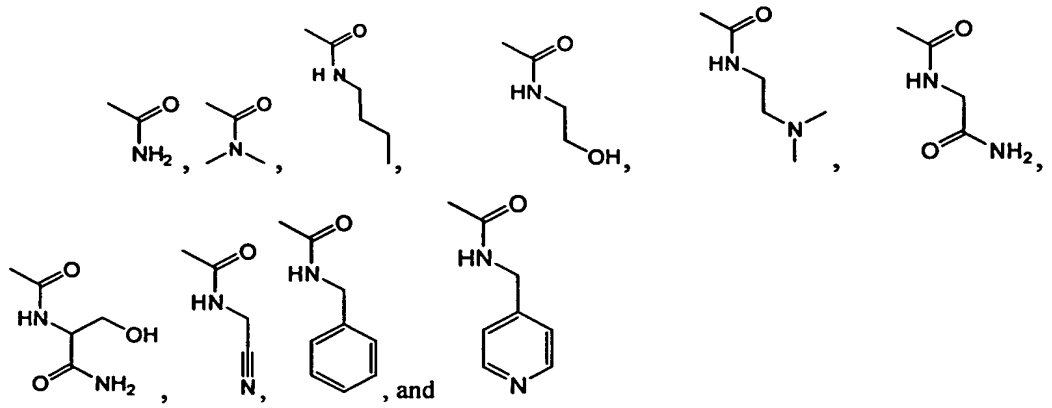


[0287] Representative substituted alkylcarbonylamino, alkyloxycarbonylamino, aminoalkyloxycarbonylamino, and arylcarbonylamino groups include, for example, those

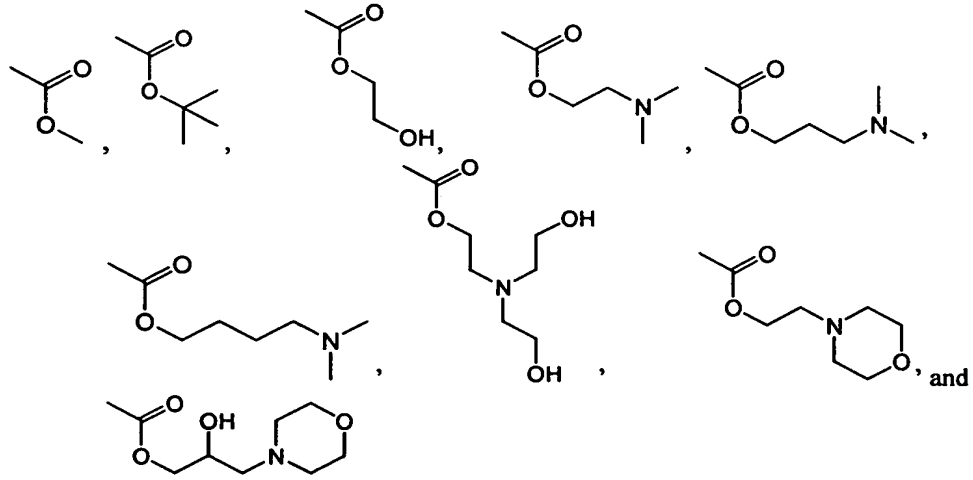
shown below. These groups can be further substituted as will be apparent to those having skill in the organic and medicinal chemistry arts in conjunction with the disclosure herein.



[0288] Representative substituted aminocarbonyl groups include, for example, those shown below. These can be further substituted by heterocyclo groups and heteroaryl groups as will be apparent to those having skill in the organic and medicinal chemistry arts in conjunction with the disclosure herein. Prefered aminocarbonyl groups include: N-(2-cyanoethyl)carboxamide, N-(3-methoxypropyl)carboxamide, N-cyclopropyl-carboxamide, N-(2-hydroxy-isopropyl)carboxamide, methyl 2-carbonylamino-3-hydroxypropanoate, N-(2-hydroxypropyl)carboxamide, N-(2-hydroxy-isopropyl)-carboxamide, N-[2-hydroxy-1-(hydroxymethyl)ethyl]-carboxamide, N-(2-carbonylaminoethyl)acetamide, N-(2-(2-pyridyl)ethyl)-carboxamide, N-(2-pyridylmethyl)carboxamide, N-(oxolan-2-ylmethyl)-carboxamide, N-(4-hydroxypyrrolidin-2-yl)carboxamide, N-[2-(2-hydroxyethoxy)ethyl]-carboxamide, N-(4-hydroxycyclohexyl)carboxamide, N-[2-(2-oxo-4-imidazolinyl)-ethyl]-carboxamide, N-(carbonylaminomethyl)acetamide, N-(3-pyrrolidinylpropyl)-carboxamide, N-[1-(carbonylaminomethyl)pyrrolidin-3-yl]acetamide, N-(2-morpholin-4-ylethyl)-carboxamide, N-[3-(2-oxopyrrolidinyl)propyl]carboxamide, 4-methyl-2-oxopiperazine-carbaldehyde, N-(2-hydroxy-3-pyrrolidinylpropyl)-carboxamide, N-(2-hydroxy-3-morpholin-4-ylpropyl)carboxamide, N-{2-[(5-cyano-2-pyridyl)amino]-ethyl}carboxamide, 3-(dimethyl-amino)pyrrolidinecarbaldehyde, N-[(5-methylpyrazin-2-yl)methyl]carboxamide, 2,2,2-trifluoro-N-(1-formylpyrrolidin-3-yl)acetamide,

[0289] 

[0290] Representative substituted alkoxycarbonyl groups include, for example, those shown below. These alkoxycarbonyl groups can be further substituted as will be apparent to those having skill in the organic and medicinal chemistry arts in conjunction with the disclosure herein.



[0291] The term "protected" with respect to hydroxyl groups, amine groups, and sulfhydryl groups refers to forms of these functionalities which are protected from undesirable reaction with a protecting group known to those skilled in the art such as those set forth in Protective Groups in Organic Synthesis, Greene, T.W.; Wuts, P. G. M., John Wiley & Sons, New York, NY, (3rd Edition, 1999) which can be added or removed using the procedures set forth therein. Examples of protected hydroxyl groups include, but are not limited to, silyl ethers such as those obtained by reaction of a hydroxyl group with a reagent such as, but not limited to, t-butyldimethyl-chlorosilane, trimethylchlorosilane, triisopropylchlorosilane, triethylchlorosilane; substituted methyl and ethyl ethers such as, but not limited to methoxymethyl ether, methythiomethyl ether, benzyloxymethyl ether, t-

butoxymethyl ether, 2-methoxyethoxymethyl ether, tetrahydropyranyl ethers, 1-ethoxyethyl ether, allyl ether, benzyl ether; esters such as, but not limited to, benzoylformate, formate, acetate, trichloroacetate, and trifluoracetate. Examples of protected amine groups include, but are not limited to, amides such as, formamide, acetamide, trifluoroacetamide, and benzamide; imides, such as phthalimide, and dithiosuccinimide; and others. Examples of protected sulfhydryl groups include, but are not limited to, thioethers such as S-benzyl thioether, and S-4-picolyl thioether; substituted S-methyl derivatives such as hemithio, dithio and aminothio acetals; and others.

[0292] It should be understood that the organic compounds according to the invention may exhibit the phenomenon of tautomerism. As the chemical structures within this specification can only represent one of the possible tautomeric forms, it should be understood that the invention encompasses any tautomeric form of the drawn structure.

[0293] A "pharmaceutically acceptable salt" includes a salt with an inorganic base, organic base, inorganic acid, organic acid, or basic or acidic amino acid. As salts of inorganic bases, the invention includes, for example, alkali metals such as sodium or potassium; alkaline earth metals such as calcium and magnesium or aluminum; and ammonia. As salts of organic bases, the invention includes, for example, trimethylamine, triethylamine, pyridine, picoline, ethanolamine, diethanolamine, and triethanolamine. As salts of inorganic acids, the instant invention includes, for example, hydrochloric acid, hydroboric acid, nitric acid, sulfuric acid, and phosphoric acid. As salts of organic acids, the instant invention includes, for example, formic acid, acetic acid, trifluoroacetic acid, fumaric acid, oxalic acid, tartaric acid, maleic acid, citric acid, succinic acid, malic acid, methanesulfonic acid, benzenesulfonic acid, and p-toluenesulfonic acid. As salts of basic amino acids, the instant invention includes, for example, arginine, lysine and ornithine. Acidic amino acids include, for example, aspartic acid and glutamic acid.

[0294] As used herein, the term "pharmaceutically acceptable ester" refers to esters, which hydrolyze in vivo and include those that break down readily in the human body to leave the parent compound or a salt thereof. Suitable ester groups include, for example, those derived from pharmaceutically acceptable aliphatic carboxylic acids, particularly alkanoic, alkenoic, cycloalkanoic and alkanedioic acids, in which each alkyl or alkenyl moiety advantageously has not more than 6 carbon atoms. Representative examples of particular

esters include, but are not limited to, formates, acetates, propionates, butyrates, acrylates and ethylsuccinates.

[0295] The term "pharmaceutically acceptable prodrugs" as used herein refers to those prodrugs of the compounds of the present invention which are, within the scope of sound medical judgment, suitable for use in contact with the tissues of humans and lower animals without undue toxicity, irritation, allergic response, and the like, commensurate with a reasonable benefit/risk ratio, and effective for their intended use, as well as the zwitterionic forms, where possible, of the compounds of the invention. The term "prodrug" refers to compounds that are rapidly transformed in vivo to yield the parent compound of the above formula, for example by hydrolysis in blood. A thorough discussion is provided in T. Higuchi and V. Stella, Pro-drugs as Novel Delivery Systems, Vol. 14 of the A.C.S. Symposium Series, and in Edward B. Roche, ed., Bioreversible Carriers in Drug Design, American Pharmaceutical Association and Pergamon Press, 1987, both of which are incorporated herein by reference.

[0296] The methods of the invention are useful in treating "allergic diseases," which is accomplished in the same way as other immunotherapeutic methods described herein. An "allergen" refers to a substance (antigen) that can induce an allergic or asthmatic response in a susceptible subject. The list of allergens is enormous and can include pollens, insect venoms, animal dander, dust, fungal spores, and drugs (e.g. penicillin).

[0297] "Asthma" refers to a disorder of the respiratory system characterized by inflammation, narrowing of the airways and increased reactivity of the airways to inhaled agents. Asthma is frequently, although not exclusively associated with atopic or allergic symptoms.

[0298] "Immune-stimulation" or "immune potentiation" refers to the increase in cytokine production from a dendritic cell.

[0299] A "subject" or "patient" is meant to describe a human or vertabrate animal including a dog, cat, horse, cow, pig, sheep, goat, chicken, monkey, rat, and mouse.

[0300] Suitable pharmaceutically acceptable excipients include processing agents and drug delivery modifiers and enhancers, such as, for example, calcium phosphate, magnesium stearate, talc, monosaccharides, disaccharides, starch, gelatin, cellulose, methyl cellulose, sodium carboxymethyl cellulose, dextrose, hydroxypropyl-β-cyclodextrin, polyvinylpyrrolidinone, low melting waxes, ion exchange resins, and the like, as well as

combinations of any two or more thereof. Other suitable pharmaceutically acceptable excipients are described in "Remington: The Science and Practice of Pharmacy ,"Lippincott Williams and Wilkins, Baltimore, Maryland (1995), incorporated herein by reference.

[0301] Pharmaceutical compositions containing the compounds of the invention may be in any form suitable for the intended method of administration, including, for example, a solution, a suspension, or an emulsion. Liquid carriers are typically used in preparing solutions, suspensions, and emulsions. Liquid carriers contemplated for use in the practice of the present invention include, for example, water, saline, pharmaceutically acceptable organic solvent(s), pharmaceutically acceptable oils or fats, and the like, as well as mixtures of two or more thereof. The liquid carrier may contain other suitable pharmaceutically acceptable additives such as solubilizers, emulsifiers, nutrients, buffers, preservatives, suspending agents, thickening agents, viscosity regulators, stabilizers, and the like. Suitable organic solvents include, for example, monohydric alcohols, such as ethanol, and polyhydric alcohols, such as glycols. Suitable oils include, for example, soybean oil, coconut oil, olive oil, safflower oil, cottonseed oil, and the like. For parenteral administration, the carrier can also be an oily ester such as ethyl oleate, isopropyl myristate, and the like. Compositions of the present invention may also be in the form of microparticles, microcapsules, liposomal encapsulates, and the like, as well as combinations of any two or more thereof.

[0302] The compounds of the invention may be administered enterally, orally, parenterally, sublingually, by inhalation spray, rectally, or topically in dosage unit formulations containing conventional nontoxic pharmaceutically acceptable carriers, adjuvants, and vehicles as desired. For example, suitable modes of administration include oral, subcutaneous, transdermal, transmucosal, iontophoretic, intravenous, intramuscular, intraperitoneal, intranasal, subdural, rectal, and the like. Topical administration may also involve the use of transdermal administration such as transdermal patches or ionophoresis devices. The term parenteral as used herein includes subcutaneous injections, intravenous, intramuscular, intrasternal injection, or infusion techniques.

[0303] Injectable preparations, for example, sterile injectable aqueous or oleaginous suspensions may be formulated according to the known art using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation may also be a sterile injectable solution or suspension in a nontoxic parenterally acceptable diluent or solvent, for example, as a solution in 1,3-propanediol. Among the acceptable vehicles and solvents that

may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

[0304] Suppositories for rectal administration of the drug can be prepared by mixing the drug with a suitable nonirritating excipient such as cocoa butter and polyethylene glycols that are solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum and release the drug.

[0305] Solid dosage forms for oral administration may include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound may be admixed with at least one inert diluent such as sucrose lactose or starch. Such dosage forms may also comprise, as is normal practice, additional substances other than inert diluents, e.g., lubricating agents such as magnesium stearate. In the case of capsules, tablets, and pills, the dosage forms may also comprise buffering agents. Tablets and pills can additionally be prepared with enteric coatings.

[0306] Liquid dosage forms for oral administration may include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs containing inert diluents commonly used in the art, such as water. Such compositions may also comprise adjuvants, such as wetting agents, emulsifying and suspending agents, cyclodextrins, and sweetening, flavoring, and perfuming agents.

[0307] Effective amounts of the compounds of the invention generally include any amount sufficient to detectably treat viral infections.

[0308] Successful treatment of a subject in accordance with the invention may result in the inducement of a reduction or alleviation of symptoms in a subject afflicted with a medical or biological disorder to, for example, halt the further progression of the disorder, or the prevention of the disorder.

[0309] The amount of active ingredient that may be combined with the carrier materials to produce a single dosage form will vary depending upon the host treated and the particular mode of administration. It will be understood, however, that the specific dose level for any particular patient will depend upon a variety of factors including the activity of the specific compound employed, the age, body weight, general health, sex, diet, time of

administration, route of administration, rate of excretion, drug combination, and the severity of the particular disease undergoing therapy. The therapeutically effective amount for a given situation can be readily determined by routine experimentation and is within the skill and judgment of the ordinary clinician.

[0310] For purposes of the present invention, a therapeutically effective dose will generally be from about 0.1 mg/kg/day to about 1000 mg/kg/day, preferably from about 1 mg/kg/day to about 20 mg/kg/day, which may be administered in one or multiple doses with or without an antigen as described herein.

[0311] The compounds of the present invention can also be administered in the form of liposomes. As is known in the art, liposomes are generally derived from phospholipids or other lipid substances. Liposomes are formed by mono- or multilamellar hydrated liquid crystals that are dispersed in an aqueous medium. Any non-toxic, physiologically acceptable and metabolizable lipid capable of forming liposomes can be used. The present compositions in liposome form can contain, in addition to a compound of the present invention, stabilizers, preservatives, excipients, and the like. The preferred lipids are the phospholipids and phosphatidyl cholines (lecithins), both natural and synthetic. Methods to form liposomes are known in the art. See, for example, Prescott, Ed., Methods in Cell Biology, Volume XIV, Academic Press, New York, N.W., p. 33 et seq (1976).

[0312] While the compounds of the invention can be administered as the sole active pharmaceutical agent, they can also be used in combination with one or more other agents used in the treatment of disorders. Representative agents useful in combination with the compounds of the invention for the treatment of viral infections include, for example, Interferon, Ribavirin, and the like.

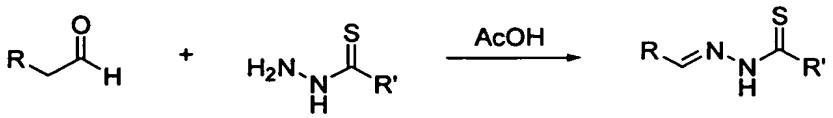
[0313] When additional active agents are used in combination with the compounds of the present invention, the additional active agents may generally be employed in therapeutic amounts as indicated in the Physicians' Desk Reference (PDR) 57th Edition (2003), PDR/Medical Economics Company, which is incorporated herein by reference, or such therapeutically useful amounts as would be known to one of ordinary skill in the art.

[0314] The compounds of the invention and the other therapeutically active agents can be administered at the recommended maximum clinical dosage or at lower doses. Dosage levels of the active compounds in the compositions of the invention may be varied so as to obtain a desired therapeutic response depending on the route of administration, severity

of the disease and the response of the patient. The combination can be administered as separate compositions or as a single dosage form containing both agents. When administered as a combination, the therapeutic agents can be formulated as separate compositions that are given at the same time or different times, or the therapeutic agents can be given as a single composition.

[0315] General procedure for the preparation of thiosemicarbazones

[0316] Scheme 1



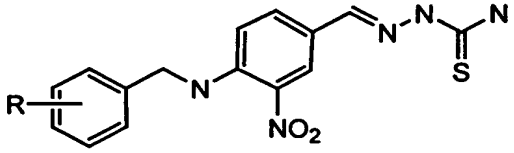
[0317] A solution of aldehyde (1.0 equiv.) and thiosemicarbazide (1.05 equiv.) in acetic acid was stirred overnight. Excess of acetic acid was removed to give a residue, which was washed with ethanol, or purified by preparative-HPLC to give the thiosemicarbazone.

[0318] Scheme 2

[0319] A solution of aldehyde (1.0 equiv.), thiosemicarbazide (1.05 equiv.) and acetic acid (0.1 equiv.) in methanol was stirred overnight. Methanol was removed to give a residue, which was worked up as in Scheme 1.

[0320] Scheme 3

[0321] To a solution of {[(1E)-1-aza-2-(4-fluoro-3-nitrophenyl)vinyl]amino}-aminomethane-1-thione in ethanol was added an arylamine (2.1 equiv.). The solution was stirred at room temperature until the starting fluoride disappeared. The solution was purified to the product.

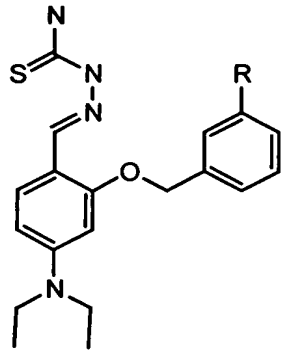


[0322] Scheme 4

[0323] A mixture of 4-(diethylamino)-2-hydroxybenzaldehyde (1 equiv.), benzylic bromide (1.2 equiv.) and powder potassium carbonate in ethanol was stirred at room temperature for 2 days. Ethanol was removed, and the residue was dissolved in ethyl acetate and water. The organic layer was washed with aqueous $NaHCO_3$ and brine, dried over

Na2SO4., and concentrated. The residue was purified on silica gel eluting with ethyl acetate/hexane to give 4-(diethylamino)-2-benzoxylic-benzaldehyde.

[0324] The aldehydes were converted to thiosemicarbazones according to Scheme 2.



[0325] Scheme 5

[0326] A solution of 3,4-difluorobenzenecarbonitrile (1 equiv.), amine (1.5 equiv.) and DIEA (2 equiv.) in NMP was heated in a Smith Microwave (Personal Chemistry) for 30 minutes. The reaction mixture was purified on silica gel to give 4-substituted 3-fluorobenzenecarbonitrile.

[0327] To a solution of nitrile in toluene at –78 °C was added DIBAL-H (1 M in toluene, 1.5 equiv.). The reaction mixture was warmed to rt, and stirred for 16 h, and quenched with methanol/ethyl acetate/brine (1:1:4). After being stirred at rt for 30 min, the solution was extracted with ethyl acetate (3x). The combined organic layers were washed with aqueous $NaHCO_3$, brine and concentrated. The aldehyde was purified on silica gel or directly converted to thiosemicarbazones (Scheme 2).

[0328] Scheme 6

[0329] A solution of 2,4,5-trifluorobenzenecarbonitrile (1 equiv.) and 4-arylpiperazine (1.2 equiv.) and DIEA (1.2 equiv.) in THF was heated at 80 °C for 2 hours. The mixture was purified on silica gel to give 4-substituted 2,5-difluorobenzenecarbonitrile.

[0330] Scheme 7

[0331] To an alcohol (1.0 equiv) was added potassium t-butoxide in THF (1 M, 1.1 equiv). After 5 minutes, the solution was added to a solution of 4-N-substituted-2,5-difluorobenzenecarbonitrile (1 equiv.) in THF. The reaction mixture was stirred at rt overnight and quenched with aqueous ammonium chloride. The aqueous layer was extracted

with ethyl acetate (3x). The combined organic layers were washed with brine, and concentrated to give a residue, which was purified to give 4-N-substituted-2-O-substituted-5-fluorobenzenecarbonitrile.

[0332] 4-N-substituted-2-O-substituted-5-fluorobenzenecarbonitrile was reduced with DIBAL-H to give a 4-N-substituted-2-O-substituted-5-fluorobenzaldehyde according to procedure in Scheme 5.

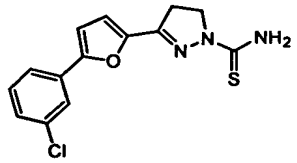
[0333] The aldehyde was converted to the corresponding thiosemicarbazone using Scheme 2.

[0334] Scheme 8

[0335] A solution of 4-N-substituted-2,5-difluorobenzenecarbonitrile (1 equiv.), amine (1.5 equiv.) and DIEA (2 equiv.) in NMP was heated in a Smith Microwave (Personal Chemistry) for 30 minutes. The reaction mixture was purified on silica gel to give 4-N-substituted-2-N-substituted-5-fluorobenzenecarbonitrile.

[0336] 4-N-substituted-2-N-substituted-5-fluorobenzenecarbonitrile was reduced with DIBAL-H according to procedure described in Scheme 5 to give 4-N-substituted-2-N-substituted-5-fluorobenzaldehyde.

[0337] Preparation of amino{3-[5-(3-chlorophenyl)(2-furyl)](2-pyrazolinyl)}methane-1-thione



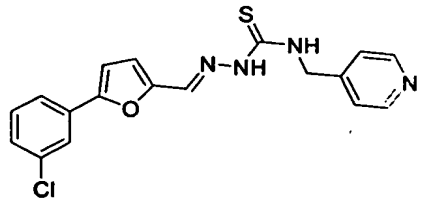
[0338] To a solution of 5-(3-chlorophenyl)furan-2-carbaldehyde (1.0 equiv.) in THF at 0 °C was added MeMgBr in ether (3.0 equiv.) and stirred for 45 min. The reaction was quenched with water, diluted with ether and filtered through Celite. The organic layer was separated and washed with brine, dried over $MgSO_4$, and concentrated to give the 1-[5-(3-chlorophenyl)-2-furyl]ethan-1-ol.

[0339] To a solution of secondary alcohol(1.0 equiv.) in CH_2Cl_2 was added MnO_2 (10 equiv.). The reaction was stirred overnight, filtered through Celite, and concentrated to give 1-[5-(3-chlorophenyl)-2-furyl]ethan-1-one.

[0340] To a mixture of ketone (1.0 equiv.), paraformaldehyde (2.0 equiv.), and dimethylamine hydrochloride (2.0 equiv) and molecular sieves in ethanol was added concentrated hydrochloric acid (cat.). The reaction was refluxed overnight under nitrogen and the concentrated. A few drops of HCl was added, and the mixture was worked up with DCM and water. The organic layer was discarded. The aqueous layer was adjusted to basic and extracted with DCM (3x). The organic layer was washed with brine, dried over $MgSO_4$, and concentrated to yield 3-(dimethylamino)-1-[5-(3-chlorophenyl)(2-furyl)]propan-1-one.

[0341] Thiosemicarbazide (1.0 equiv.) was dissolved in MeOH upon heating under nitrogen. Aqueous sodium hydroxide (6 M, 9.0 equiv.) was added to the reaction. A methanol solution of 3-(dimethylamino)-1-[5-(3-chlorophenyl)(2-furyl)]propan-1-one (1.0 equiv) was then added dropwise to the reaction mixture. The solvent was removed and the residue was dissolved in DCM and washed with water, brine, dried over $MgSO_4$, and concentrated. The final compound was purified by preparative-HPLC to give amino{3-[5-(3-chlorophenyl)(2-furyl)](2-pyrazolinyl)}methane-1-thione; LC/MS m/z 306.2 (MH+); Rt =3.06 minutes .

[0342] Scheme 9



[0343] To a solution of 4-pyridylmethylamine (1.0 equiv.) and triethylamine (2.0 equiv.) in $CHCl_3$ was added CS_2 (1.0 equiv.)) and stirred overnight. The reaction was cooled to 0 °C and ethyl chloroformate (1.0 equiv.) was added dropwise. The reaction was stirred for 15 min at 0 °C and then stirred at room temperature for 2 hrs followed by addition of (tert-butyl)oxycarbohydrazide (1.2 equiv.). After stirring for an addition hour the mixture was washed with aqueous citric acid (5%), saturated $NaHCO_3$, brine, dried over $MgSO_4$, and concentrated. The desired Boc protected thiosemicarbazide was purified using column chromatography.

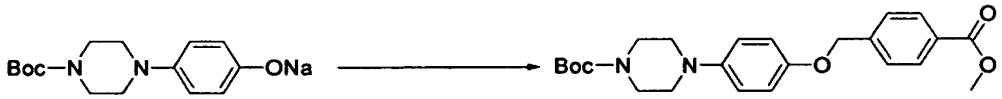
[0344] To a solution of Boc protected thiosemicarbazide (1.0 equiv.) dissolved in DCM was added HCl in dioxane (2M, 8.3 equiv.) and stirred for 15 min. MeOH is then added to dissolve the precipitate, followed by addition of the furfural, and small amount of

acetic acid (0.5 mL). The mixture is stirred overnight and the solvents are removed to give a residue purified by preparative-HPLC to give the thiosemicarbazone.

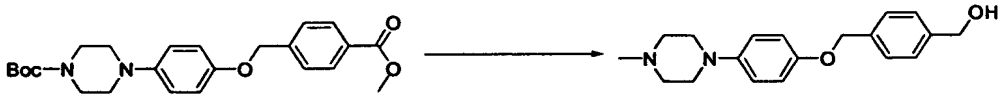
[0345] Synthesis of 4-[4-(4-methylpiperazin-1-yl)phenoxymethyl]benzaldehyde

[0346] To a solution of 4-piperazin-1-yl phenol (1 equivalent) in $CHCl_3$, cooled to 0 °C, was added di-*t*-butyl dicarbonate (1 equivalent) in $CHCl_3$ drop-wise. The solution was stirred at 0 °C for 1 hour before removing from the cold bath and stirring at ambient temperatures for 18 hours. The organic solution was washed aqueous $NaHCO_3$ and brine dried over $MgSO_4$ and concentrated the crude material was used without purification.

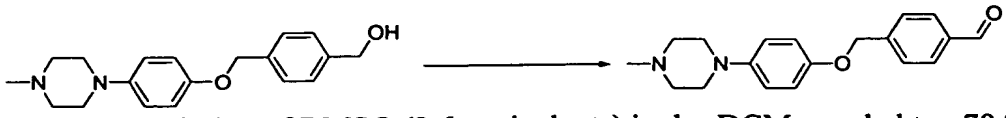
[0347] A solution of the resulting 4-(1-BOC-piperazin-4-yl)phenol (1 equivalent) in dry CH_3CN was slowly added drop-wise to a slurry of NaH (1 equivalent) in dry CH_3CN at room temperature under N_2. The slurry was stirred at room temperature for 2 hours before the solids were filtered and washed with Et_2O.



[0348] Sodium 4-(1-BOC-piperazin-4-yl)phenoxide (1 equivalent) and methyl 4-bromomethylbenzoate (1 equivalent) were combined in dry acetone and heated to reflux at 60 °C for 18 hours. The slurry was filtered and the filtrate was then concentrated to provide the crude methyl 4-[4-(1-BOC-piperazin-4-yl)phenoxymethyl]benzoate, which was used without purification.



[0349] To a slurry of $LiAlH_4$ (4 equivalents) in dry THF, cooled to 0 °C under N_2, was slowly added drop-wise a solution of methyl 4-[4-(1-BOC-piperazin-4-yl)phenoxymethyl]benzoate (1 equivalent) in dry THF. Once the addition was complete, the slurry was heated to reflux at 80 °C for 1 hour. The slurry was subsequently cooled to 0 °C and treated with water, 10% aq. NaOH and with water again. The resulting solids were filtered, and the filtrate was diluted with chloroform, washed with brine, dried over $MgSO_4$ and concentrated, providing the crude 4-[4-(4-methylpiperazin-1-yl)phenoxymethyl]benzyl alcohol which was used without purification.



[0350] To a solution of DMSO (2.6 equivalents) in dry DCM , cooled to –78 °C under N_2 was added oxalyl chloride (1.1 equivalents) in DCM drop-wise. The solution was stirred at –78 °C for 5 minutes before a solution of 4-[4-(4-methylpiperazin-1-yl)phenoxymethyl]benzyl alcohol (1 equivalent) in DCM was added drop-wise, and allowed to stir at –78 °C for another 30 minutes. Triethylamine (2.5 equivalents) was slowly dripped in before allowing the solution to reach ambient temperatures. The solution was washed with aqueous $NaHCO_3$ and brine, dried over $MgSO_4$ and concentrated to provide the crude 4-[4-(4-methylpiperazin-1-yl)phenoxymethyl]benzaldehyde which was converted to thiosemicarbazones according to Scheme 2.

[0351] Characterization and Purification Methods

[0352] Referring to the examples that follow, compounds of the present invention were characterized by high performance liquid chromatography (HPLC) using a Waters Millenium chromatography system with a 2690 Separation Module (Milford, Massachusetts). The analytical columns were Alltima C-18 reversed phase, 4.6 x 250 mm from Alltech (Deerfield, Illinois). A gradient elution was used, typically starting with 5% acetonitrile/95% water and progressing to 100% acetonitrile over a period of 40 minutes. All solvents contained 0.1% trifluoroacetic acid (TFA). Compounds were detected by ultraviolet light (UV) absorption at either 220 or 254 nm. HPLC solvents were from Burdick and Jackson (Muskegan, Michigan), or Fisher Scientific (Pittsburg, Pennsylvania). In some instances, purity was assessed by thin layer chromatography (TLC) using glass or plastic backed silica gel plates, such as, for example, Baker-Flex Silica Gel 1B2-F flexible sheets. TLC results were readily detected visually under ultraviolet light, or by employing well known iodine vapor and other various staining techniques.

[0353] Mass spectrometric analysis was performed on one of two LCMS instruments: a Waters System (Alliance HT HPLC and a Micromass ZQ mass spectrometer; Column: Eclipse XDB-C18, 2.1 x 50 mm; solvent system: 5-95% (or 35-95%, or 65-95% or 95-95%) acetonitrile in water with 0.05%TFA; flow rate 0.8 mL/min; molecular weight range 500-1500; cone Voltage 20 V; column temperature 40°C) or a Hewlett Packard System (Series 1100 HPLC; Column: Eclipse XDB-C18, 2.1 x 50 mm; solvent system: 1-95% acetonitrile in water with 0.05%TFA; flow rate 0.4 mL/min; molecular weight range 150-850; cone Voltage

50 V; column temperature 30°C). All masses are reported as those of the protonated parent ions.

[0354] GCMS analysis was performed on a Hewlet Packard instrument (HP6890 Series gas chromatograph with a Mass Selective Detector 5973; injector volume: 1 μL; initial column temperature: 50°C; final column temperature: 250°C; ramp time: 20 minutes; gas flow rate: 1 mL/min; column: 5% phenyl methyl siloxane, Model #HP 190915-443, dimensions: 30.0 m x 25 m x 0.25 m).

[0355] Nuclear magnetic resonance (NMR) analysis was performed with a Varian 300 Mhz NMR (Palo Alto, California). The spectral reference was either TMS or the known chemical shift of the solvent. Some compound samples were run at elevated temperatures (i.e. 75°C) to promote increased sample solubility.

[0356] The purity of some of the invention compounds was assessed by elemental analysis (Desert Analytics, Tuscon, Arizona)

[0357] Melting points were determined on a Laboratory Devices Mel-Temp apparatus (Holliston, Massachusetts).

[0358] Preparative separations were carried out using a Flash 40 chromatography system and KP-Sil, 60A (Biotage, Charlottesville, Virginia), or by flash column chromatography using silica gel (230-400 mesh) packing material, or by HPLC using a C-18 reversed phase column. Typical solvents employed for the Flash 40 Biotage system and flash column chromatography were dichloromethane, methanol, ethyl acetate, hexane, acetone, aqueous hydroxyamine and triethyl amine. Typical solvents employed for the reverse phase HPLC were varying concentrations of acetonitrile and water with 0.1% trifluoroacetic acid.

[0359] Compounds of the present invention can be readily synthesized using the methods described herein, or other methods, which are well known in the art. The precursors are readily recognizable by one skilled in the art and are commercially available from Aldrich (Milwaukee, WI), Acros Organics (Pittsburgh, PA), Biosynth International (Naperville, IL), Asymchem International, Inc. (Durham, NC) Maybridge Chemical Company Ltd. (Cornwall), and/or UK Peakdale Molecular (High Peak, UK).

[0360] The compounds were named using ACD/Name v. 5.04, 2001 and Nomenclator (v. 6.0) from ChemInovation Software, Inc.

[0361] The foregoing may be better understood by reference to the following examples, which are presented for illustration and not to limit the scope of the inventive concepts.

Examples

Table 1

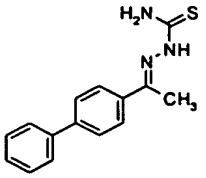
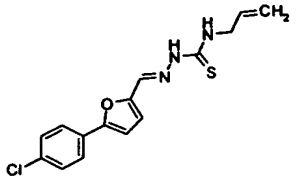
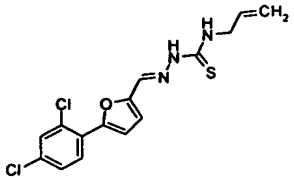
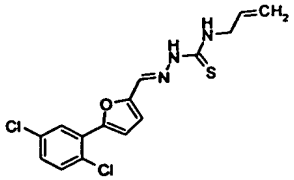
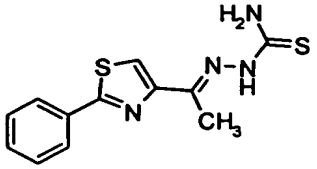
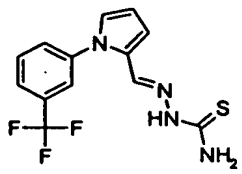
Example	Name	Structure	LC/MS (*m/z*) MH+
1	(1E)-1-(1,1'-biphenyl-4-yl)ethan-1-one thiosemicarbazone		270.4
2	5-(4-chlorophenyl)furan-2-carbaldehyde N-prop-2-enylthiosemicarbazone		320.8
3	5-(2,4-dichlorophenyl)furan-2-carbaldehyde N-prop-2-enylthiosemicarbazone		355.3
4	5-(2,5-dichlorophenyl)furan-2-carbaldehyde N-prop-2-enylthiosemicarbazone		355.3
5	(1E)-1-(2-phenyl-1,3-thiazol-4-yl)ethan-1-one thiosemicarbazone		277.4
6	1-[3-(trifluoromethyl)phenyl]-1H-pyrrole-2-carbaldehyde thiosemicarbazone		313.3

Table 1

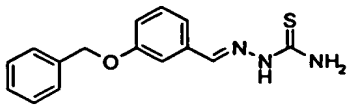
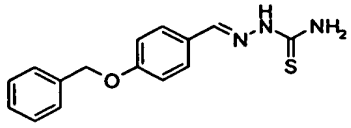
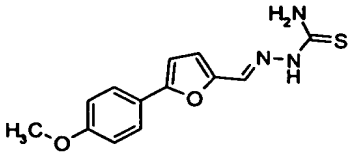
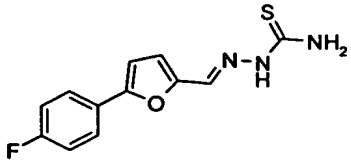
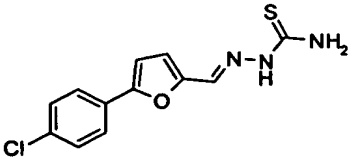
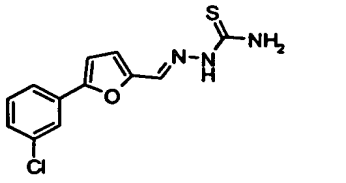
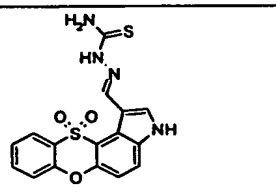
Example	Name	Structure	LC/MS (*m/z*) MH+
7	3-[(phenylmethyl)oxy]benzaldehyde thiosemicarbazone		286.4
8	4-[(phenylmethyl)oxy]benzaldehyde thiosemicarbazone		286.4
9	5-[4-(methyloxy)phenyl]furan-2-carbaldehyde thiosemicarbazone		276.3
10	5-(4-fluorophenyl)furan-2-carbaldehyde thiosemicarbazone		264.3
11	5-(4-chlorophenyl)furan-2-carbaldehyde thiosemicarbazone		280.8
12	5-(3-chlorophenyl)furan-2-carbaldehyde thiosemicarbazone		280.8
13	3H-[1,4]benzoxathiino[3,2-e]indole-1-carbaldehyde thiosemicarbazone 11,11-dioxide		373.4

Table 1

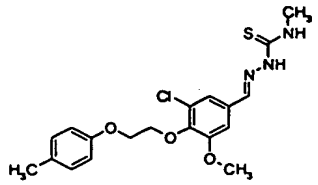
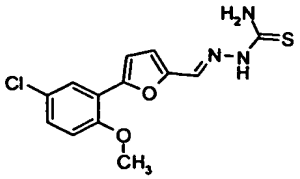
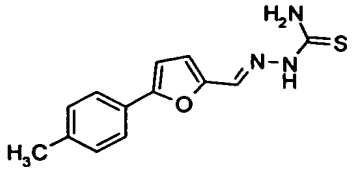
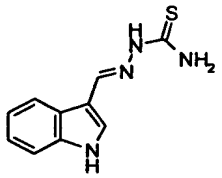
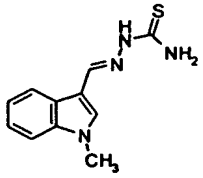
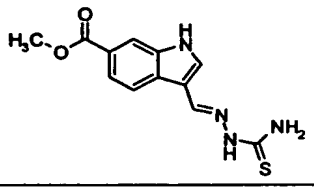
Example	Name	Structure	LC/MS (*m/z*) MH+
14	3-chloro-5-(methyloxy)-4-({2-[(4-methylphenyl)oxy]ethyl}oxy)benzaldehyde N-methylthiosemicarbazone		408.9
15	5-[5-chloro-2-(methyloxy)phenyl]furan-2-carbaldehyde thiosemicarbazone		310.8
16	5-(4-methylphenyl)furan-2-carbaldehyde thiosemicarbazone		260.3
17	1H-indole-3-carbaldehyde thiosemicarbazone		219.3
18	1-methyl-1H-indole-3-carbaldehyde thiosemicarbazone		233.3
19	methyl 3-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-1H-indole-6-carboxylate		277.3

Table 1

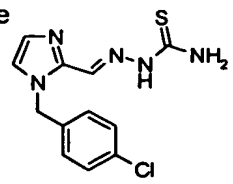
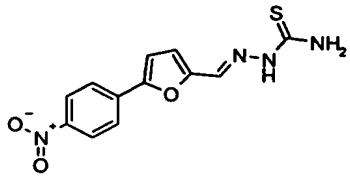
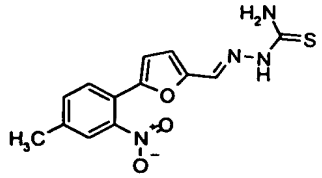
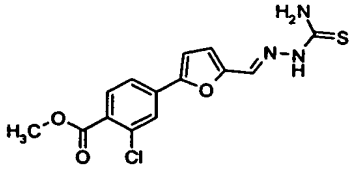
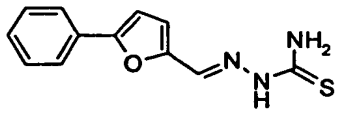
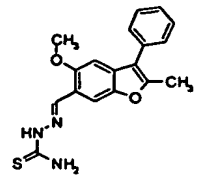
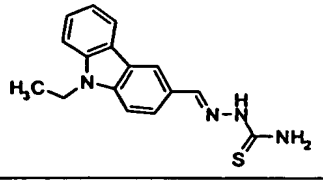
Example	Name	Structure	LC/MS (*m/z*) MH+
20	1-[(4-chlorophenyl)methyl]-1H-imidazole-2-carbaldehyde thiosemicarbazone		294.8
21	5-(4-nitrophenyl)furan-2-carbaldehyde thiosemicarbazone		291.3
22	5-(4-methyl-2-nitrophenyl)furan-2-carbaldehyde thiosemicarbazone		305.3
23	methyl 4-(5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}furan-2-yl)-2-chlorobenzoate		338.8
24	5-phenylfuran-2-carbaldehyde thiosemicarbazone		246.3
25	2-methyl-5-(methyloxy)-3-phenyl-1-benzofuran-6-carbaldehyde thiosemicarbazone		340.4
26	9-ethyl-9H-carbazole-3-carbaldehyde thiosemicarbazone		297.4

Table 1

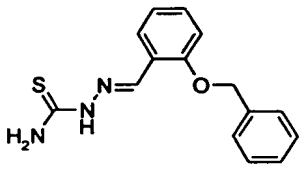
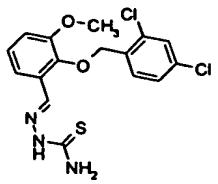
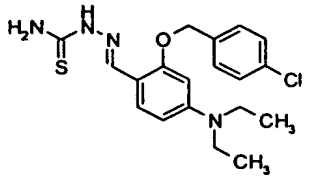
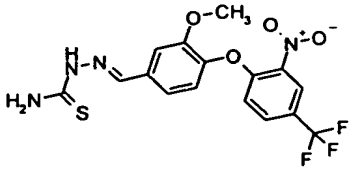
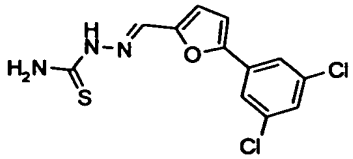
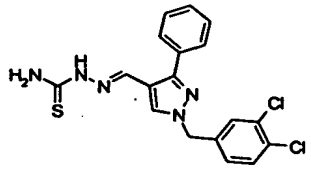
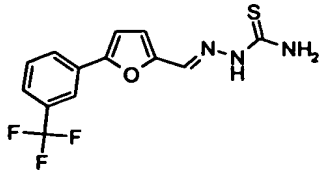
Example	Name	Structure	LC/MS (*m/z*) MH+
27	2-[(phenylmethyl)oxy]benzaldehyde thiosemicarbazone		286.4
28	2-{[(2,4-dichlorophenyl)methyl]oxy}-3-(methyloxy)benzaldehyde thiosemicarbazone		385.3
29	2-{[(4-chlorophenyl)methyl]oxy}-4-(diethylamino)benzaldehyde thiosemicarbazone		391.9
30	3-(methyloxy)-4-{[2-nitro-4-(trifluoromethyl)phenyl]oxy}benzaldehyde thiosemicarbazone		415.4
31	5-(3,5-dichlorophenyl)furan-2-carbaldehyde thiosemicarbazone		315.2
32	1-[(3,4-dichlorophenyl)methyl]-3-phenyl-1H-pyrazole-4-carbaldehyde thiosemicarbazone		405.3
33	5-[3-(trifluoromethyl)phenyl]furan-2-carbaldehyde thiosemicarbazone		314.3

Table 1

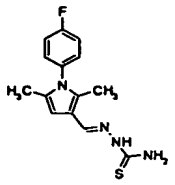
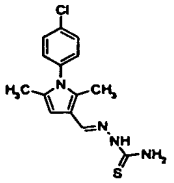
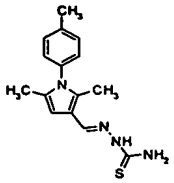
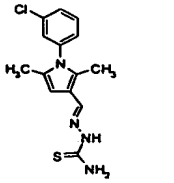
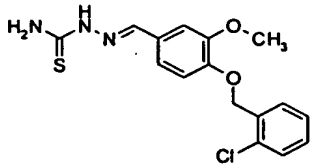
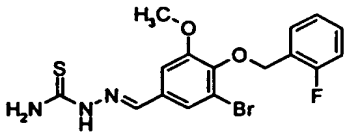
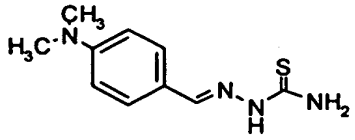
Example	Name	Structure	LC/MS (*m/z*) MH+
34	1-(4-fluorophenyl)-2,5-dimethyl-1H-pyrrole-3-carbaldehyde thiosemicarbazone		291.4
35	1-(4-chlorophenyl)-2,5-dimethyl-1H-pyrrole-3-carbaldehyde thiosemicarbazone		307.8
36	2,5-dimethyl-1-(4-methylphenyl)-1H-pyrrole-3-carbaldehyde thiosemicarbazone		287.4
37	1-(3-chlorophenyl)-2,5-dimethyl-1H-pyrrole-3-carbaldehyde thiosemicarbazone		307.8
38	4-{[(2-chlorophenyl)methyl]oxy}-3-(methyloxy)benzaldehyde thiosemicarbazone		350.8
39	3-bromo-4-{[(2-fluorophenyl)methyl]oxy}-5-(methyloxy)benzaldehyde thiosemicarbazone		413.3
40	4-(dimethylamino)benzaldehyde thiosemicarbazone		223.3

Table 1

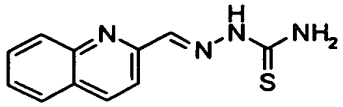
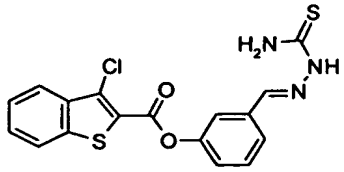
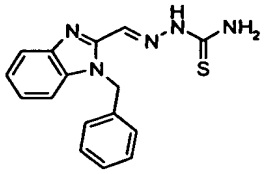
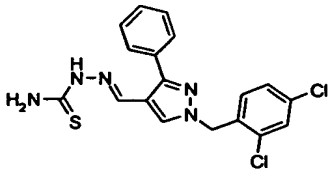
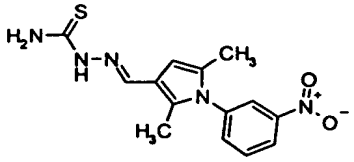
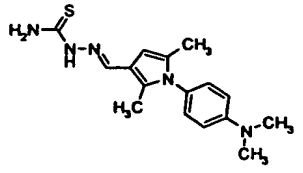
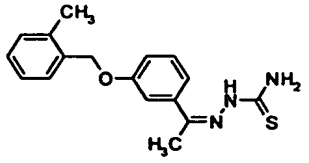
Example	Name	Structure	LC/MS (*m/z*) MH+
41	quinoline-2-carbaldehyde thiosemicarbazone		231.3
42	3-{(E)-[2-(aminocarbonothioyl)hydrazono]methyl}phenyl 3-chloro-1-benzothiophene-2-carboxylate		390.9
43	1-(phenylmethyl)-1H-benzimidazole-2-carbaldehyde thiosemicarbazone		310.4
44	1-[(2,4-dichlorophenyl)methyl]-3-phenyl-1H-pyrazole-4-carbaldehyde thiosemicarbazone		405.3
45	2,5-dimethyl-1-(3-nitrophenyl)-1H-pyrrole-3-carbaldehyde thiosemicarbazone		318.4
46	1-[4-(dimethylamino)phenyl]-2,5-dimethyl-1H-pyrrole-3-carbaldehyde thiosemicarbazone		316.4
47	(1Z)-1-(3-{[(2-methylphenyl)methyl]oxy}phenyl)ethan-1-one thiosemicarbazone		314.4

Table 1

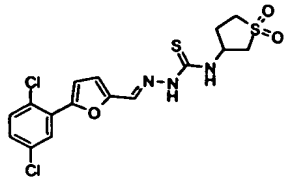
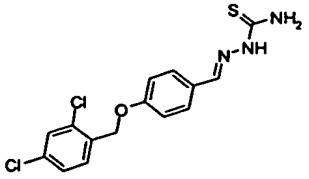
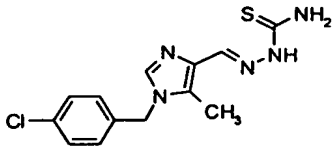
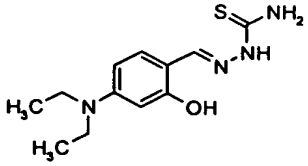
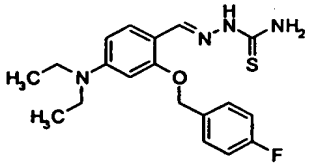
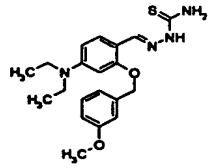
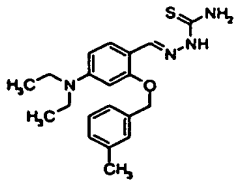
Example	Name	Structure	LC/MS (*m/z*) MH+
48	5-(2,5-dichlorophenyl)furan-2-carbaldehyde N-(1,1-dioxidotetrahydrothien-3-yl)thiosemicarbazone		433.4
49	4-{[(2,4-dichlorophenyl)methyl]oxy}benzaldehyde thiosemicarbazone		355.3
50	1-[(4-chlorophenyl)methyl]-5-methyl-1H-imidazole-4-carbaldehyde thiosemicarbazone		308.8
51	4-(diethylamino)-2-hydroxybenzaldehyde thiosemicarbazone		267.4
52	4-(diethylamino)-2-{[(4-fluorophenyl)methyl]oxy}benzaldehyde thiosemicarbazone		375.5
53	4-(diethylamino)-2-({[3-(methyloxy)phenyl]methyl}oxy)benzaldehyde thiosemicarbazone		387.5
54	4-(diethylamino)-2-{[(3-methylphenyl)methyl]oxy}benzaldehyde thiosemicarbazone		371.5

Table 1

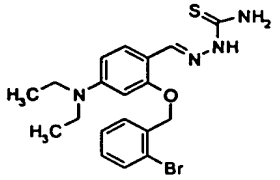
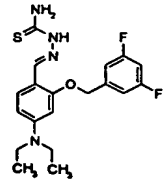
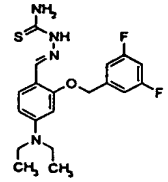
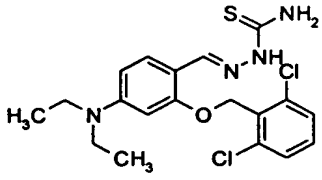
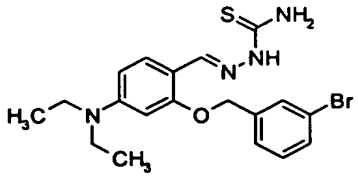
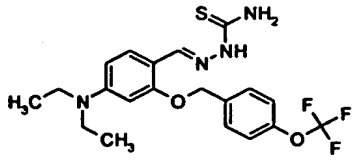
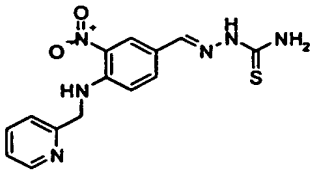
Example	Name	Structure	LC/MS (*m/z*) MH+
55	2-{[(2-bromophenyl)methyl]oxy}-4-(diethylamino)benzaldehyde thiosemicarbazone		436.4
56	4-(diethylamino)-2-{[(3,5-difluorophenyl)methyl]oxy}benzaldehyde thiosemicarbazone		393.5
57	4-(diethylamino)-2-{[(3,5-difluorophenyl)methyl]oxy}benzaldehyde thiosemicarbazone		393.5
58	2-{[(2,6-dichlorophenyl)methyl]oxy}-4-(diethylamino)benzaldehyde thiosemicarbazone		426.4
59	2-{[(3-bromophenyl)methyl]oxy}-4-(diethylamino)benzaldehyde thiosemicarbazone		436.4
60	4-(diethylamino)-2-[({4-[(trifluoromethyl)oxy]phenyl}methyl)oxy]benzaldehyde thiosemicarbazone		441.5
61	3-nitro-4-[(pyridin-2-ylmethyl)amino]benzaldehyde thiosemicarbazone		331.4

Table 1

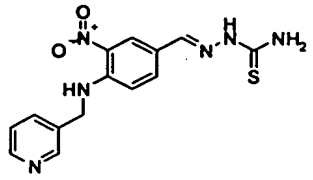
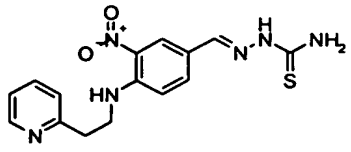
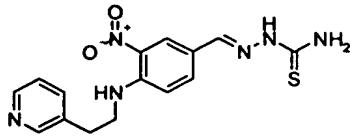
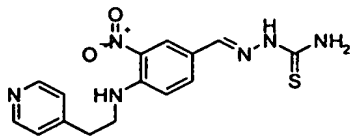
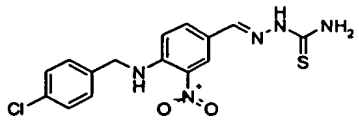
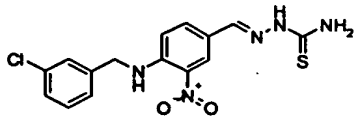
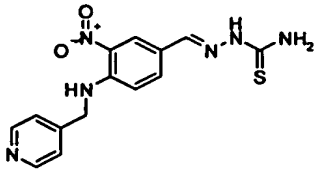
Example	Name	Structure	LC/MS (*m/z*) MH+
62	3-nitro-4-[(pyridin-3-ylmethyl)amino]benzaldehyde thiosemicarbazone		331.4
63	3-nitro-4-[(2-pyridin-2-ylethyl)amino]benzaldehyde thiosemicarbazone		345.4
64	3-nitro-4-[(2-pyridin-3-ylethyl)amino]benzaldehyde thiosemicarbazone		345.4
65	3-nitro-4-[(2-pyridin-4-ylethyl)amino]benzaldehyde thiosemicarbazone		345.4
66	4-{[(4-chlorophenyl)methyl]amino}-3-nitrobenzaldehyde thiosemicarbazone		364.8
67	4-{[(3-chlorophenyl)methyl]amino}-3-nitrobenzaldehyde thiosemicarbazone		364.8
68	3-nitro-4-[(pyridin-4-ylmethyl)amino]benzaldehyde thiosemicarbazone		331.4

Table 1

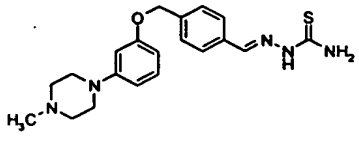
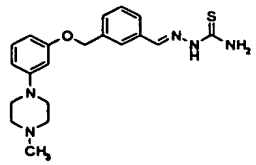
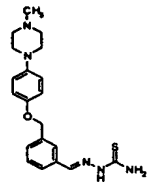
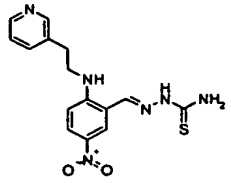
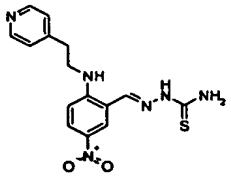
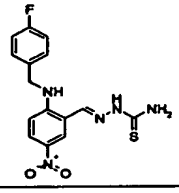
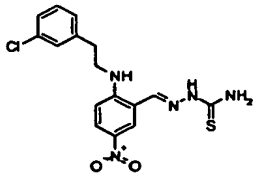
Example	Name	Structure	LC/MS (*m/z*) MH+
69	4-({[3-(4-methylpiperazin-1-yl)phenyl]oxy}methyl)benzaldehyde thiosemicarbazone		384.5
70	3-({[3-(4-methylpiperazin-1-yl)phenyl]oxy}methyl)benzaldehyde thiosemicarbazone		384.5
71	3-({[4-(4-methylpiperazin-1-yl)phenyl]oxy}methyl)benzaldehyde thiosemicarbazone		384.5
72	5-nitro-2-[(2-pyridin-3-ylethyl)amino]benzaldehyde thiosemicarbazone		345.4
73	5-nitro-2-[(2-pyridin-4-ylethyl)amino]benzaldehyde thiosemicarbazone		345.4
74	2-{[(4-fluorophenyl)methyl]amino}-5-nitrobenzaldehyde thiosemicarbazone		348.4
75	2-{[2-(3-chlorophenyl)ethyl]amino}-5-nitrobenzaldehyde thiosemicarbazone		378.9

Table 1

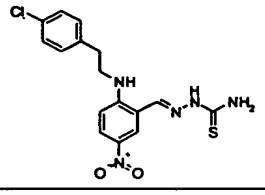
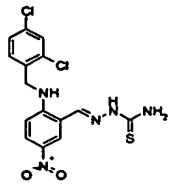
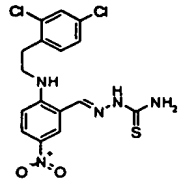
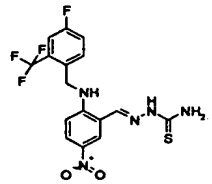
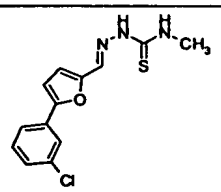
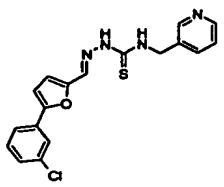
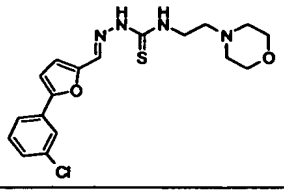
Example	Name	Structure	LC/MS (*m/z*) MH+
76	2-{[2-(4-chlorophenyl)ethyl]amino}-5-nitrobenzaldehyde thiosemicarbazone		378.9
77	2-{[(2,4-dichlorophenyl)methyl]amino}-5-nitrobenzaldehyde thiosemicarbazone		399.3
78	2-{[2-(2,4-dichlorophenyl)ethyl]amino}-5-nitrobenzaldehyde thiosemicarbazone		413.3
79	2-({[4-fluoro-2-(trifluoromethyl)phenyl]methyl}amino)-5-nitrobenzaldehyde thiosemicarbazone		416.4
80	5-(3-chlorophenyl)furan-2-carbaldehyde N-methylthiosemicarbazone		294.8
81	5-(3-chlorophenyl)furan-2-carbaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone		371.9
82	5-(3-chlorophenyl)furan-2-carbaldehyde N-(2-morpholin-4-ylethyl)thiosemicarbazone		393.9

Table 1

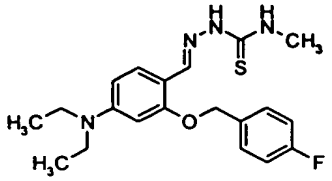
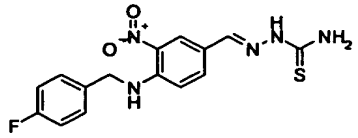
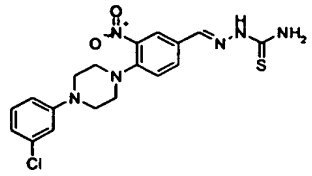
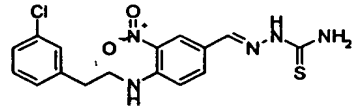
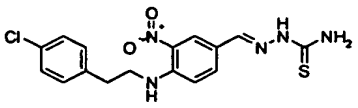
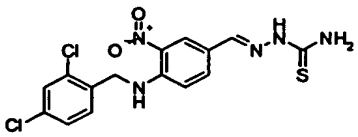
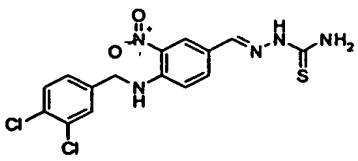
Example	Name	Structure	LC/MS (*m/z*) MH+
83	4-(diethylamino)-2-{[(4-fluorophenyl)methyl]oxy}benzaldehyde N-methylthiosemicarbazone		389.5
84	4-{[(4-fluorophenyl)methyl]amino}-3-nitrobenzaldehyde thiosemicarbazone		348.4
85	4-[4-(3-chlorophenyl)piperazin-1-yl]-3-nitrobenzaldehyde thiosemicarbazone		419.9
86	4-{[2-(3-chlorophenyl)ethyl]amino}-3-nitrobenzaldehyde thiosemicarbazone		378.9
87	4-{[2-(4-chlorophenyl)ethyl]amino}-3-nitrobenzaldehyde thiosemicarbazone		378.9
88	4-{[(2,4-dichlorophenyl)methyl]amino}-3-nitrobenzaldehyde thiosemicarbazone		399.3
89	4-{[(3,4-dichlorophenyl)methyl]amino}-3-nitrobenzaldehyde thiosemicarbazone		399.3

Table 1

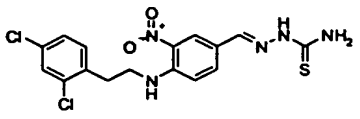
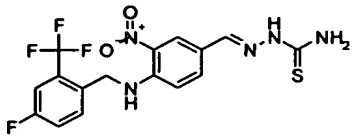
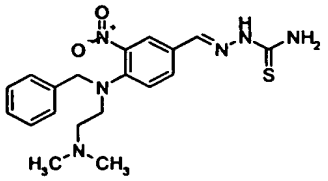
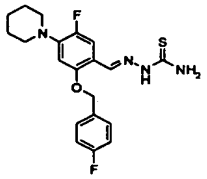
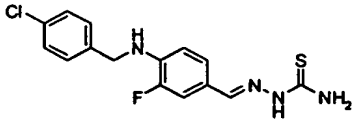
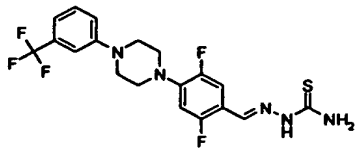
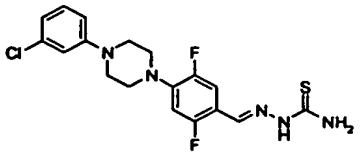
Example	Name	Structure	LC/MS (*m/z*) MH+
90	4-{[2-(2,4-dichlorophenyl)ethyl]amino}-3-nitrobenzaldehyde thiosemicarbazone		413.3
91	4-({[4-fluoro-2-(trifluoromethyl)phenyl]methyl}amino)-3-nitrobenzaldehyde thiosemicarbazone		416.4
92	4-[[2-(dimethylamino)ethyl](phenylmethyl)amino]-3-nitrobenzaldehyde thiosemicarbazone		401.5
93	5-fluoro-2-{[(4-fluorophenyl)methyl]oxy}-4-piperidin-1-ylbenzaldehyde thiosemicarbazone		405.5
94	4-{[(4-chlorophenyl)methyl]amino}-3-fluorobenzaldehyde thiosemicarbazone		337.8
95	2,5-difluoro-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone		444.4
96	4-[4-(3-chlorophenyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone		410.9

Table 1

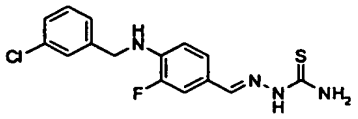
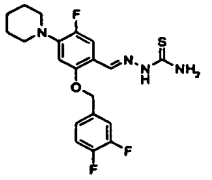
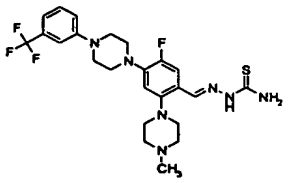
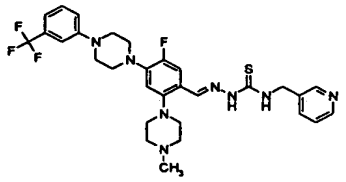
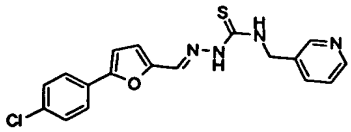
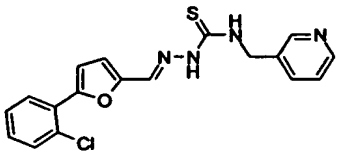
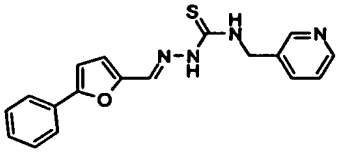
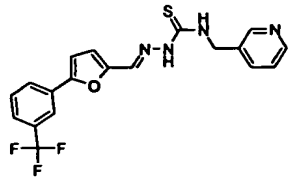
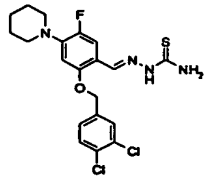
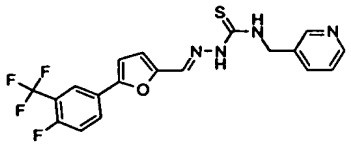
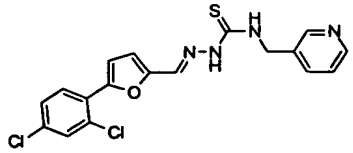
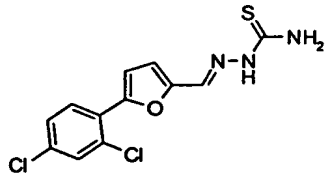
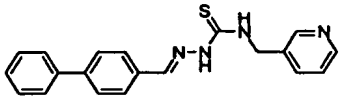
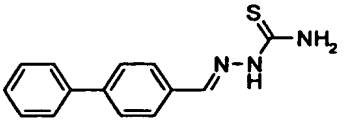
Example	Name	Structure	LC/MS (*m/z*) MH+
97	4-{[(3-chlorophenyl)methyl]amino}-3-fluorobenzaldehyde thiosemicarbazone		337.8
98	2-{[(3,4-difluorophenyl)methyl]oxy}-5-fluoro-4-piperidin-1-ylbenzaldehyde thiosemicarbazone		423.5
99	5-fluoro-2-(4-methylpiperazin-1-yl)-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone		524.6
100	5-fluoro-2-(4-methylpiperazin-1-yl)-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone		615.7
101	5-(4-chlorophenyl)furan-2-carbaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone		371.9
102	5-(2-chlorophenyl)furan-2-carbaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone		371.9
103	5-phenylfuran-2-carbaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone		337.4

Table 1

Example	Name	Structure	LC/MS (*m/z*) MH+
104	5-[3-(trifluoromethyl)phenyl]furan-2-carbaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone		405.4
105	2-{[(3,4-dichlorophenyl)methyl]oxy}-5-fluoro-4-piperidin-1-ylbenzaldehyde thiosemicarbazone		456.4
106	5-[4-fluoro-3-(trifluoromethyl)phenyl]furan-2-carbaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone		423.4
107	5-(2,4-dichlorophenyl)furan-2-carbaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone		406.3
108	5-(2,4-dichlorophenyl)furan-2-carbaldehyde thiosemicarbazone		315.2
109	1,1'-biphenyl-4-carbaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone		347.5
110	1,1'-biphenyl-4-carbaldehyde thiosemicarbazone		256.3

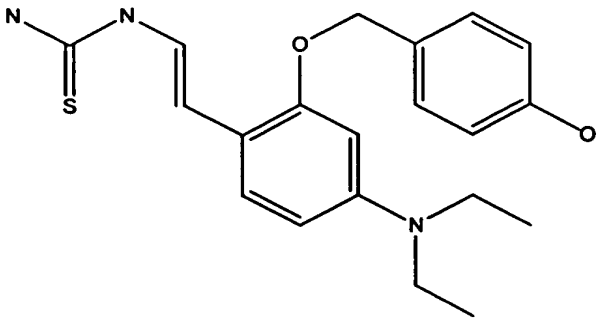
[0362] Each of the Example compounds of Table 1 was synthesized and assayed as described above. Each of these Example compounds displayed an IC_{50} value of less than 10

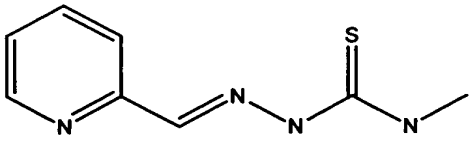
μM with respect to HCV. Many of the compounds displayed an IC_{50} value of less than or equal to 1 μM or less than or equal to 0.1 μM. Many of these compounds exhibited IC_{50} values of less than or equal to 0.050 μM, less than or equal to 0.030 μM, less than or equal to 0.025 μM, or less than or equal to 0.010 μM. For this reason, each of the R groups of any of the Example compounds is preferred. Additionally, because of the excellent inhibition activity of each of the Example compounds, each of these compounds is individually preferred and is preferred as a member of a group that includes any or all of the other compounds and each Example compound is preferred in methods of inhibiting HCV and in methods of treating biological conditions mediated by HCV activity, as well as modulating immunopotentiation to be used as a vaccine adjuvant. Each of the Example compounds is also preferred for use in preparation of medicaments for vaccine adjuvants, immunopotentiation, inhibiting HCV and in treating biological conditions mediated therefrom.

[0363] Candidate small molecule immuno-potentiators can be identified *in vitro*. Compounds are screened *in vitro* for their ability to stimulate human peripheral blood mononuclear cells to produce cytokines (e.g. TNF-alpha and IL-12 p40). HCV antivirals were identified having this activity. These small molecule immuno-potentiators have potential utility as adjuvants and immuno-therapeutics.

[0364] Example 111

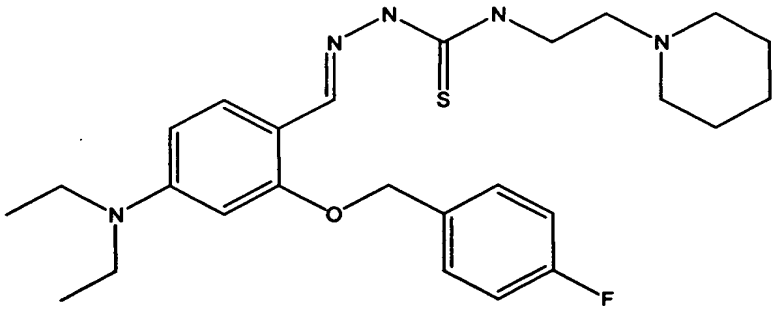
[0365] TNF-alpha production by human PBMC was measured using a commercial ELISA from supernatants of cells stimulated with the indicated compounds for 18 to 24 hours All test compounds were used at a final concentration of 5 μM/ml. Untreated PBMC (Cells) and LPS (0.1 ng/ml), CPG (10 ng/ml) and/or ALTTE (5 μM/ml) treated PBMC served as negative and positive controls, respectively. The following HCV antiviral compounds induced TNF and IL-12 production by human PBMC *in vitro*. The results are shown in Figure 1.





[0366] Example 112

[0367] The following thiosemicarbazone was tested at concentrations of 10 μM, 5 μM, 2.5 μM, and 1.25 μM for its ability to induce cytokines from human PBMC. Multi-cytokine analysis was performed using the Luminex system on culture supernatants following 18 h incubation with the compound. The results are presented as percent of cytokine production following stimulation with an optimal does (10 ng/ml) of LPS. The cytokines measured were: IL-6, TNF-α, IFN-γ, and IL-10.



[0368] The results are shown in Figure 2.

[0369] Table 2. Cytokine secretion of hPBMC after stimulation with thiosemicarbazone compounds.

Table 2

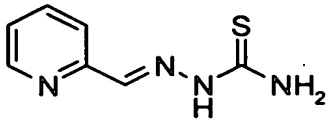
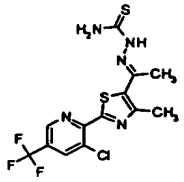
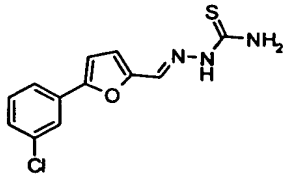
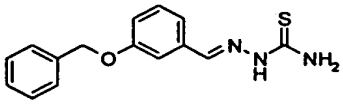
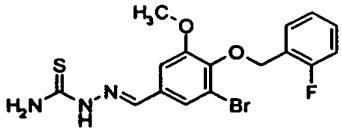
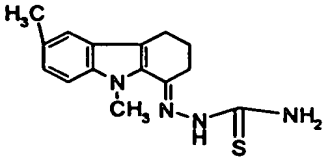
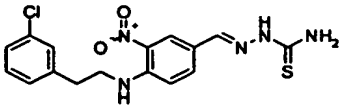
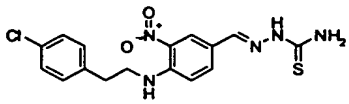
Example	Structure	Name	LC/MS (*mz*) MH+	TNFa production (ng/10^6 cells /ml)
113		pyridine-2-carbaldehyde thiosemicarbazone	181.2	2.34
114		(1E)-1-{2-[3-chloro-5-(trifluoromethyl)pyridin-2-yl]-4-methyl-1,3-thiazol-5-yl}ethan-1-one thiosemicarbazone	394.8	1.7
12		5-(3-chlorophenyl)furan-2-carbaldehyde thiosemicarbazone	280.8	2.32
7		3-[(phenylmethyl)oxy]benzaldehyde thiosemicarbazone	286.4	0
39		3-bromo-4-{[(2-fluorophenyl)methyl]oxy}-5-(methyloxy)benzaldehyde thiosemicarbazone	413.3	5
115		(1E)-6,9-dimethyl-2,3,4,9-tetrahydro-1H-carbazol-1-one thiosemicarbazone	287.4	1.25
86		4-{[2-(3-chlorophenyl)ethyl]amino}-3-nitrobenzaldehyde thiosemicarbazone	378.9	5

Table 2

Example	Structure	Name	LC/MS (*mz*) MH+	TNFa production (ng/10^6 cells /ml)
87		4-{[2-(4-chlorophenyl)ethyl]amino}-3-nitrobenzaldehyde thiosemicarbazone	378.9	1.25

[0370] *High Throughput Screening (*HTS*) for small molecule immune potentiators; SMIPs:* Attention is drawn to Figure 3. Various compounds were evaluated for their ability to produce cytokines in response to the small molecule compounds using a modified sandwich ELISA. Compounds are screened for their TNF inducing. "Hits" are selected based on their TNF-inducing activity relative to an optimal dose a strong TNF inducer. The robustness of the assay and low backgrounds have allowed for the routine selection of hits with ~10% of this activity which is normally between 5-10X background (cells alone). Selected hits are then subjected to confirmation for their ability to induce cytokines from multiple donors at decreasing concentrations. Those compounds with consistent activity at or below 5μM are considered confirmed.

[0371] *Dual functional HCV anti-virals and immune potentiators*: Thiosemicarbazones compounds with and without anti-HCV activity were screened for their capacity to activate immune cells. Structural analogs of this scaffold have been tested for their ability to induce cytokines from human PBMC and murine splenocytes. Figure 4 shows results from representative assays for human TNF-alpha (black bars) and IL-12 p40 (gray bars) presented as the % of LPS (1 μg/ml) activity. All compounds were tested at a final concentration of 5 μM except for poly I:C (PIC) and the 1806 oligodinucleotide (CpG) which were used at 10 μg/ml and 10 ng/ml respectively. Numerous thiosemicarbazones were tested with this approach and some of these have previously been shown to have anti-HCV acivity in separate assays but have weak or absent SMIP activity. Others (e.g. Example 113) possess potent SMIP activity but have weak or absent anti-HCV effects. Finally compounds, such as Example 29, possess both SMIP and anti-HCV activity in independent assays.

[0372] *Quantification of HCV replicon RNA in cell lines (HCV Cell Based Assay):* Cell lines, including Huh-11-7 or Huh 9-13, harboring HCV replicons (Lohmann, et al

Science 285:110-113, 1999) are seeded at $5x10^3$ cells/well in 96 well plates and fed media containing DMEM (high glucose), 10% fetal calf serum, penicillin-streptomycin and non-essential amino acids. Cells are incubated in a 5% CO_2 incubator at 37 °C. At the end of the incubation period, total RNA is extracted and purified from cells using Qiagen Rneasy 96 Kit (Catalog No. 74182). To amplify the HCV RNA so that sufficient material can be detected by an HCV specific probe (below), primers specific for HCV (below) mediate both the reverse transcription (RT) of the HCV RNA and the amplification of the cDNA by polymerase chain reaction (PCR) using the TaqMan One-Step RT-PCR Master Mix Kit (Applied Biosystems catalog no. 4309169). The nucleotide sequences of the RT-PCR primers, which are located in the NS5B region of the HCV genome, are the following:

[0373] HCV Forward primer "RBNS5bfor"

[0374] 5'GCTGCGGCCTGTCGAGCT:

[0375] HCV Reverse primer "RBNS5Brev":

[0376] 5'CAAGGTCGTCTCCGCATAC

[0377] Detection of the RT-PCR product was accomplished using the Applied Biosystem (ABI) Prism 7700 Sequence Detection System (SDS) that detects the fluorescence that is emitted when the probe, which is labeled with a fluorescence reporter dye and a quencher dye, is processed during the PCR reaction. The increase in the amount of fluorescence is measured during each cycle of PCR and reflects the increasing amount of RT-PCR product. Specifically, quantification is based on the threshold cycle, where the amplification plot crosses a defined fluorescence threshold. Comparison of the threshold cycles of the sample with a known standard provides a highly sensitive measure of relative template concentration in different samples (ABI User Bulletin #2 December 11, 1997). The data is analyzed using the ABI SDS program version 1.7. The relative template concentration can be converted to RNA copy numbers by employing a standard curve of HCV RNA standards with known copy number (ABI User Bulletin #2 December 11, 1997).

[0378] The RT-PCR product was detected using the following labeled probe:

[0379] 5' FAM-CGAAGCTCCAGGACTGCACGATGCT-TAMRA

[0380] FAM = Fluorescence reporter dye.

[0381] TAMRA = Quencher dye.

[0382] The RT reaction is performed at 48 °C for 30 minutes followed by PCR. Thermal cycler parameters used for the PCR reaction on the ABI Prism 7700 Sequence Detection System were: one cycle at 95 °C, 10 minutes followed by 35 cycles each of which included one incubation at 95 °C for 15 seconds and a second incubation for 60 °C for 1 minute.

[0383] To normalize the data to an internal control molecule within the cellular RNA, we perform RT-PCR on the cellular messenger RNA glyceraldehydes-3-phosphate dehydrogenase (GAPDH). The GAPDH copy number is very stable in the cell lines used. GAPDH RT-PCR is performed on the same exact RNA sample from which the HCV copy number is determined. The GAPDH primers and probes, as well as the standards with which to determine copy number, is contained in the ABI Pre-Developed TaqMan Assay Kit (catalog no. 4310884E). The ratio of HCV/GAPDH RNA is used to calculate the activity of compounds evaluated for inhibition of HCV RNA replication.

[0384] Activity of compounds as inhibitors of HCV replication (Cell based Assay) in replicon containing Huh-7 cell lines: The effect of a specific anti-viral compound on HCV replicon RNA levels in Huh-11-7 or 9-13 cells, cells was determined by comparing the amount of HCV RNA normalized to GAPDH (e.g. the ratio of HCV/GAPDH) in the cells exposed to compound versus cells exposed to the 0% inhibition and the100% inhibition controls. Specifically, cells were seeded at 5x 103 cells/well in a 96 well plate and were incubated either with: 1) media containing 1% DMSO (0% inhibition control), 2) 100 international units, IU/ml Interferon-alpha 2b in media/1%DMSO or 3) media/1%DMSO containing a fixed concentration of compound. 96 well plates as described above were then incubated at 37 °C for 3 days (primary screening assay) or 4 days (IC_{50} determination). Percent inhibition was defined as:

[0385] % Inhibition= [100-((S-C2)/C1-C2))]x100

[0386] where:

[0387] S= the ratio of HCV RNA copy number/GAPDH RNA copy number in the sample

[0388] C1= the ratio of HCV RNA copy number/GAPDH RNA copy number in the 0% inhibition control (media/1%DMSO)

[0389] C2= the ratio of HCV RNA copy number/GAPDH RNA copy number in the 100% inhibition control (100 IU/ml Interferon-alpha 2b)

[0390] The dose-response curve of the inhibitor was generated by adding compound in serial, three-fold dilutions over three logs to wells starting with the highest concentration of a specific compound at 10uM and ending with the lowest concentration of 0.01uM. Further dilution series (1uM to 0.001uM for example) was performed if the IC_{50} value was not in the linear range of the curve. IC_{50} was determined based on the IDBS Activity Base program using Microsoft Excel "XL Fit" in which A=100% inhibition value (100IU/ml Interferon-alpha 2b), B= 0% inhibition control value (media/1%DMSO) and C= midpoint of the curve as defined as C=(B-A/2)+A. A, B and C values are expressed as the ratio of HCV RNA/GAPDH RNA as determined for each sample in each well of a 96 well plate as described above. For each plate the average of 4 wells were used to define the 100% and 0% inhibition values.

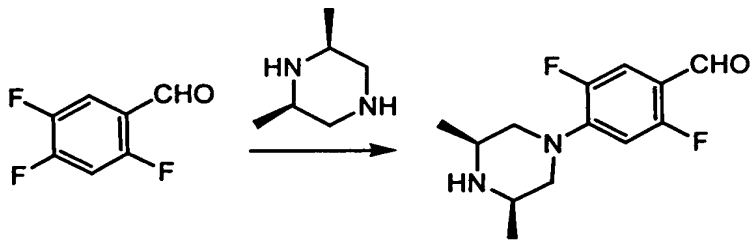
[0391]

[0392] Further Examples

[0393] Additional exemplary compounds were using the exmplary synthesis reactions set forth below. By varying starting materials and/or intermediates of the schemes below, those skilled in the art can readily synthesize the variants presented in the table 3 as well as others.

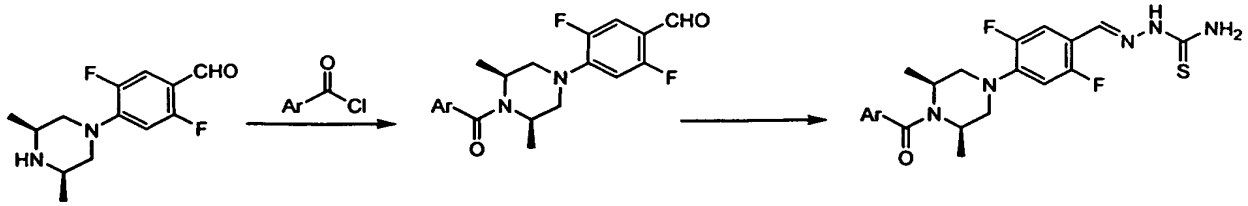
[0394]

[0395] Scheme 10: Preparation Of Difluorophenyl Thiosemicarbazone Derivatives



[0396] To a solution of 2,4,5-trifluorobenzaldehyde (1 eq) in ethyl acetate at room temperature was added 2,6-dimehtylpiperazine (2 eq). After being stirred overnight, the solution was washed with water, aqueous sodium bicarbonate, brine and dried, and purified on silica gel to give 4-(cis-3,5-dimethylpiperazinyl)-2,5-difluorobenzaldehyde.

[0397]



[0398] General procedure: To a solution of 4-(cis-3,5-dimethylpiperazinyl)-2,5-difluorobenzaldehyde (1 equiv) and triethylamine (1.2 eq) in DCM at room temperature was added arylcarboxylic chloride (1.1 eq). After 1 hour, acetic acid (10 equiv) and thiosemicarbazide (1.2 eq) were added. The mixture was purified with prep-HPLC to give the 4-(4-{(1E)-2-[(aminothioxomethyl)amino]-2-azavinyl}-2,5-difluorophenyl)-cis-2,6-dimethylpiperazinyl aryl ketone.

[0399] Scheme 11: Preparation Of Pyridine Thiosemicarbazone Derivatives

[0400] 6-Substitution:

[0401] R = various piperazines

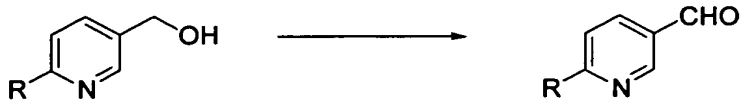
[0402] To the 6-chloro pyridine (7.2 mmol) was added ACN (15 mL) followed by DIPEA (15.9 mmol). To the solution was added the appropriate piperazine (8.0 mmol). The reaction was heated to 50 °C. Once the reaction was complete, the solution was concentrated under reduced pressure and diluted with EtOAc. The organics were washed with sat. aq. $NaHCO_3$ (x2), H_2O (x2), brine (x1), dried (Na_2SO_4), filtered, and concentrated under reduced pressure to yield the appropriate crude pyridine.

[0403] Reduction to alcohol:

[0404] The nitrile (1.9 mmol) in DCM (5 mL) was cooled to 0 °C. To the solution was added DIBAL (4.83 mmol – 1.5 M soln. in toluene) dropwise. Once the reaction was complete, it was quenched with sat. aq. NH_4Cl. The solution was diluted with DCM and H_2O

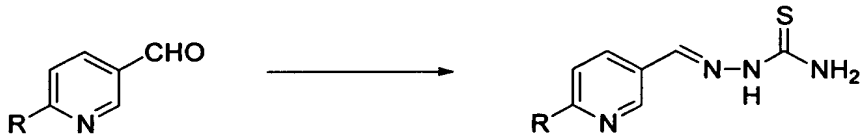
and filtered washing with DCM and H_2O. The separated aqueous layer was extracted with DCM (x3). The combined organics were washed with sat. aq. NH_4Cl (x2), H_2O (x1), brine (x1), dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give the crude alcohol.

[0405] Oxidation to aldehyde:



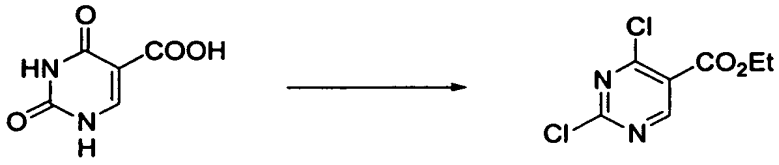
[0406] To the alcohol (0.35 mmol) in DCM (5 mL) was added MnO_2 (4.7 mmol). Once the reaction was complete, it was filtered through Celite. The filtrate was concentrated under reduced pressure to yield the crude aldehyde.

[0407] Synthesis of Thiosemicarbazone:



[0408] To the aldehyde (1.0 mmol) was added AcOH (5 mL) followed by thiosemicarbazide (1.0 mmol). Once the reaction was complete, the solution was concentrated under reduced pressure aided by toluene azeotrope. The remaining crude product was purified by prep LC to yield the pure thiosemicarbazone.

[0409] Scheme 12: Preparation of Pyrimidine thiosemicarbazone derivatives



[0410] A suspension of 5-carboxyuracil (126 mmol) in $POCl_3$ (150 mL) and DMF (126 mmol) was refluxed until the solution became homogeneous. The $POCl_3$ was removed by evaporation under reduced pressure aided by toluene azeotrope. To the remaining brown tar was added DCM (200 mL). The mixture was cooled to –25 °C and absolute EtOH (200

mL) was slowly added keeping the internal temperature below –12 °C. Once the reaction was complete, sat. aq. $NaHCO_3$ (200 mL) was added slowly keeping the internal temperature below –12 °C. Solid $NaHCO_3$ was added portionwise to adjust pH to 7-8. Organics were separated and the aqueous layer was extracted with DCM (x2). The combined organics were washed with sat. aq. $NaHCO_3$ (x2), sat. brine (x1), then dried (Na_2SO_4), filtered, and evaporated under reduced pressure to yield the crude pyrimidine. The crude product was chromatographed using 10% EtOAc in hexanes to yield the pure pyrimidine.

[0411] 4-Substitution:

[0412] R = dimethylamine, N-methyl-piperazine, N-iPr-piperazine

[0413] Ethyl 2,4-dichloropyrimidine-5-carboxylate (31.7 mmol) and triethylamine (34.9 mmol) were dissolved in DCM (150 mL) and cooled to 0 °C. The amine (31.7 mmol) was added slowly keeping the internal temperature under 5 °C. Once the reaction was complete, water (50 mL) was added. The separated organic layer was washed with sat. brine (x1), dried (Na_2SO_4), filtered, and concentrated under reduced pressure to yield the crude 4-substituted pyrimidine. The crude product was chromatographed using 20% EtOAc in hexanes to yield the pure pyrimidine.

[0414] 4-Substition:

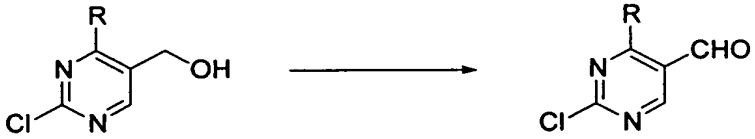
[0415] Ethyl 2,4-dichloropyrimidine-5-carboxylate (3.2 mmol) in MeOH (10 mL) was cooled to 0 °C. To the cooled solution was added NaOMe (3.2 mmol – 0.5 M soln. in MeOH). Once the reaction was complete, the solution was concentrated under reduced pressure and diluted with EtOAc. The organics were washed with H_2O (x2), sat. brine (x1),

dried (Na_2SO_4), filtered, and concentrated under reduced pressure to yield the crude 4-methoxy pyrimidine.

[0416] Reduction to alcohol:

[0417] The ester (1.9 mmol) in DCM (5 mL) was cooled to 0 °C. To the solution was added DIBAL (4.83 mmol – 1.5 M soln. in toluene) dropwise. Once the reaction was complete, it was quenched with sat. aq. NH_4Cl. The solution was diluted with DCM and H_2O and filtered washing with DCM and H_2O. The separated aqueous layer was extracted with DCM (x3). The combined organics were washed with sat. aq. NH_4Cl (x2), H_2O (x1), brine (x1), dried (Na_2SO_4), filtered, and concentrated under reduced pressure to give the crude alcohol.

[0418] Oxidation to aldehyde:



[0419] To the alcohol (0.35 mmol) in DCM (5 mL) was added MnO_2 (4.7 mmol). Once the reaction was complete, it was filtered through Celite. The filtrate was concentrated under reduced pressure to yield the crude aldehyde.

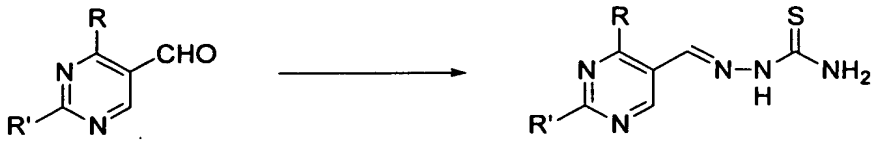
[0420] 2-Substitution:

[0421] R' = various piperazine and piperidine derivatives

[0422] To the 2-chloro pyrimidine (1.6 mmol) in ACN (5 mL) was added DIPEA (3.2 mmol) followed by the appropriate piperazine or piperidine derivative (1.7 mmol). The

solution was heated to 50 °C. Once the reaction was complete, the solution was concentrated under reduced pressure and diluted with EtOAc. The organics were washed with sat. aq. NaHCO3 (x2), H2O (x2), brine (x1), dried (Na2SO4), filtered, and concentrated under reduced pressure to yield the appropriate crude pyrimidine.

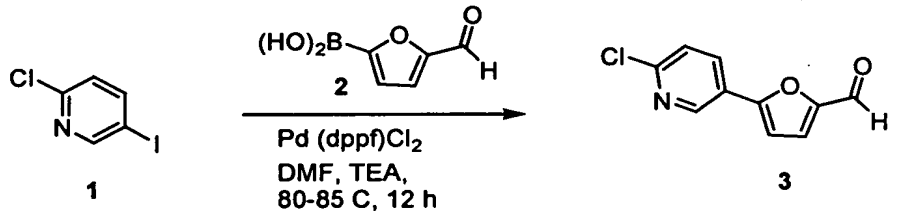
[0423] Synthesis of Thiosemicarbazone:



[0424] To the aldehyde (1.0 mmol) was added AcOH (5 mL) followed by thiosemicarbazide (1.0 mmol). Once the reaction was complete, the solution was concentrated under reduced pressure aided by toluene azeotrope. The remaining crude product was purified by prep LC to yield the pure thiosemicarbazone.

[0425] Scheme 13: Preparation of Furan thiosemicarbazone derivatives

[0426] Preparation of 5-(6-Chloro-pyridin-3-yl)-furan-2-carbaldehyde (3)

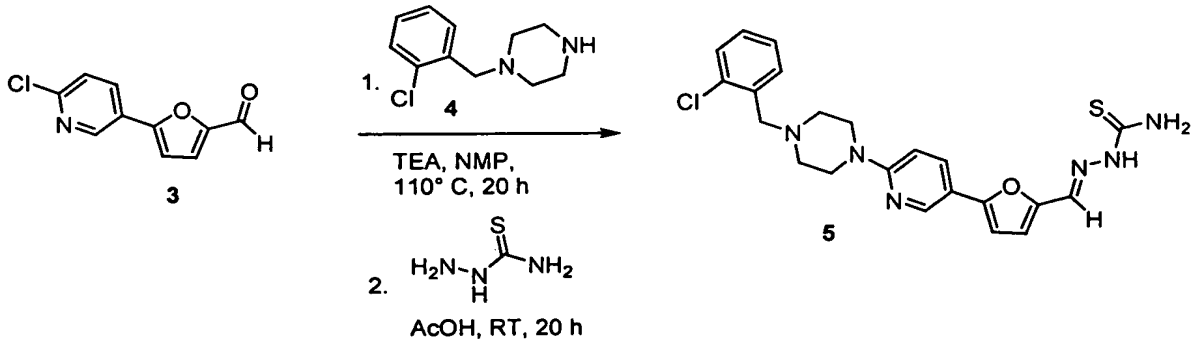


Reagent	MW	EQ	g/ml	mmol
2-Chloro-5-iodo-pyridine	239.4	1.1	1.88 g	7.86
Boronic Acid 2	140	1.0	1 g	7.15
$Pd(dppf)Cl_2$	816.63	0.03	10 mg	0.21
TEA	101.19	1.5	1.5 ml	10.72
DMF (dry & sparged with argon for 5 min.)			14 ml	

[0427] The 2-chloro-5-iodo-pyridine 1 (1.88g, 7.86mmol), furan-2-carbaldehyde-5-boronic acid 2 (1g, 7.15mmol) and $Pd(dppf)Cl_2$ catalyst (10mg, 0.21mmol) were weighted out and added to a 25ml vial. The DMF was sparged with argon for 5-10 minutes and added to the reaction followed by TEA (1.5ml, 10.72mmol). The reaction was lightly bubbled with argon. The vial was flushed with argon, capped tight and shaken at 75° C. Analytical samples were taken as needed to follow the progress of the reaction. The

reaction was flushed with argon as a precaution against oxygen. After 3.5 hours, the reaction had reached completion by HPLC. Immediately, the reaction was diluted with EtOAc (150-200ml), filtered, washed with 1N NaOH (15ml), sat. $NaHCO_3$ (2x15ml), water (15 ml), brine (15ml) and dried with Na_2SO_4. The organic layer was filtered through a plug of silica (1 inch high), and the silica was flushed with EtOAc (50ml). The combined organics were concentrated under vacuum to a solid (1.54g). The crude solid was purified by flash chromatography eluting with EtOAc/Hexane (4:6 v/v). The purified fractions were combined and evaporated under reduced pressure to give pure product (0.81g) in 55% yield.

[0428] Preparation of 5-{6-[4-(2-Chloro-benzyl)-piperazin-1-yl]-pyridin-3-yl}-furan-2-thiosemicarbazone (5)



Reagent	MW	EQ	g/ml	mmol
2-Chloropyridine 3	207.6	1.0	20.7 mg	0.1
Piperazine 2	210.7	2.5	53 mg	0.25
TEA	101.19	3.0	42 ul	0.3
NMP			0.3 ml	
Thiosemicarbazone	91.14	2.2	20 mg	0.22
AcOH gal.			120 ul	

[0429] The 5-(6-Chloro-pyridin-3-yl)-furan-2-carbaldehyde 3 (20.7mg, 0.1mmol), 1-(2-Chloro-benzyl)-piperazine 4 (53mg, 0.25mmol), TEA (42ul, 0.3mmol) and NMP (300ul) were added to a 2ml vial. The vial was flushed with argon, capped tight and shaken at 110° C. Analytical samples were taken as needed to follow the progress of the reaction. The reaction was flushed with argon as a precaution against oxygen. After ~20 hours, the reaction had reached completion by HPLC and LCMS. Thiosemicarbazone (20mg, 0.22mmol) and AcOH (120ul) were added to the reaction and shaken for 20 hours. The crude reaction was purified by prep. HPLC. The crude reaction was passed through a

Teflon syringe filter, and the clear filtrate was injected on a preparative HPLC. The purification used a 20x50 mm Ultro 120 C18 column running a 22 ml/min 2% gradient (AcCN/water, 0.1% TFA) for 16 min. The purified fractions were lyophilized to dryness to give 3.2 mg of pure product as the TFA salt (14% yield and 87% purity).

TABLE 3

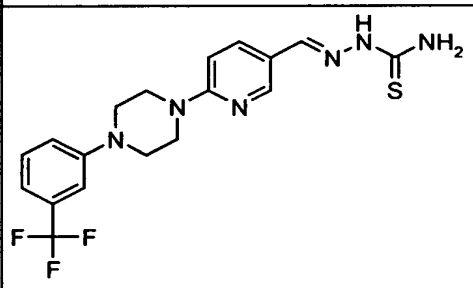
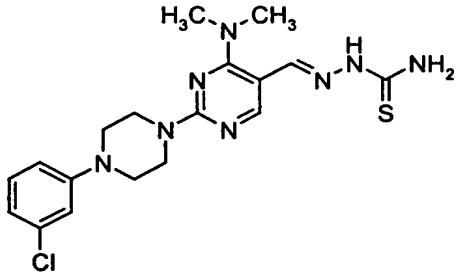
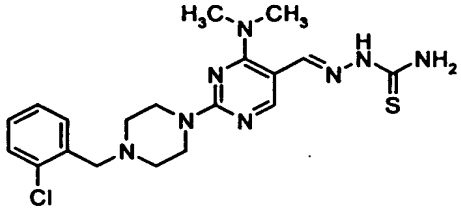
	Structure	Name	MH+
116		6-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}nicotinaldehyde thiosemicarbazone	409
117		2-[4-(3-chlorophenyl)piperazin-1-yl]-4-(dimethylamino)pyrimidine-5-carbaldehyde thiosemicarbazone	420
118		2-[4-(2-chlorobenzyl)piperazin-1-yl]-4-(dimethylamino)pyrimidine-5-carbaldehyde thiosemicarbazone	434

TABLE 3

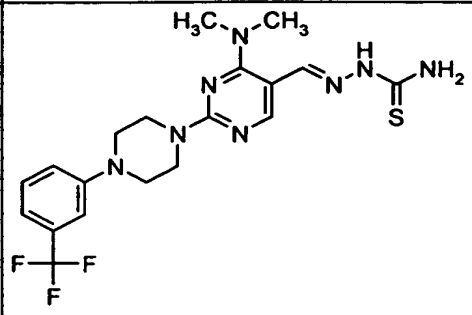
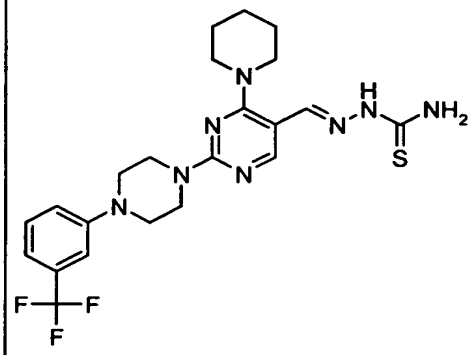
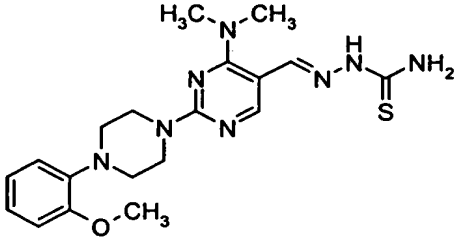
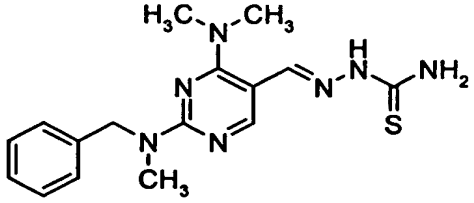
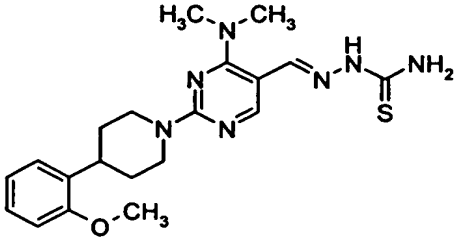
	Structure	Name	MH+
119		4-(dimethylamino)-2-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}pyrimidine-5-carbaldehyde thiosemicarbazone	454
120		4-piperidin-1-yl-2-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}pyrimidine-5-carbaldehyde thiosemicarbazone	494
121		4-(dimethylamino)-2-[4-(2-methoxyphenyl)piperazin-1-yl]pyrimidine-5-carbaldehyde thiosemicarbazone	416
122		2-[benzyl(methyl)amino]-4-(dimethylamino)pyrimidine-5-carbaldehyde thiosemicarbazone	344
123		4-(dimethylamino)-2-[4-(2-methoxyphenyl)piperidin-1-yl]pyrimidine-5-carbaldehyde thiosemicarbazone	415

TABLE 3

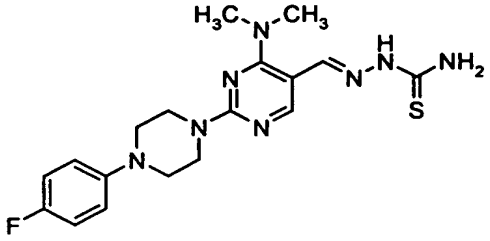
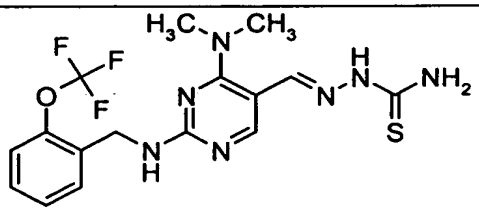
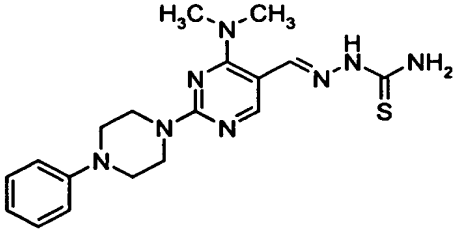
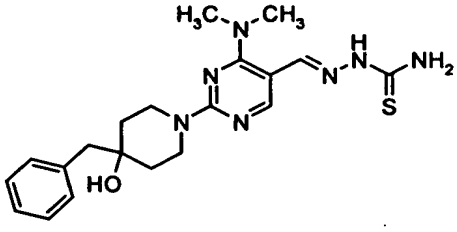
	Structure	Name	MH+
124		4-(dimethylamino)-2-[4-(4-fluorophenyl)piperazin-1-yl]pyrimidine-5-carbaldehyde thiosemicarbazone	404
125		4-(dimethylamino)-2-[4-(4-fluorobenzyl)piperazin-1-yl]pyrimidine-5-carbaldehyde thiosemicarbazone	418
126		2-(4-benzylpiperazin-1-yl)-4-(dimethylamino)pyrimidine-5-carbaldehyde thiosemicarbazone	400
127		4-(dimethylamino)-2-{[2-(trifluoromethoxy)benzyl]amino}pyrimidine-5-carbaldehyde thiosemicarbazone	414
128		4-(dimethylamino)-2-(4-phenylpiperazin-1-yl)pyrimidine-5-carbaldehyde thiosemicarbazone	386
129		2-(4-benzyl-4-hydroxypiperidin-1-yl)-4-(dimethylamino)pyrimidine-5-carbaldehyde thiosemicarbazone	415

TABLE 3

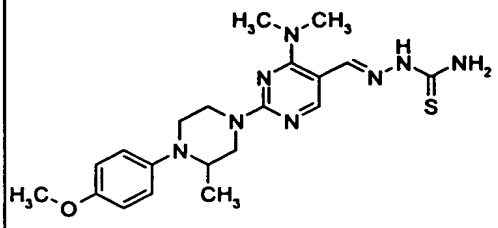
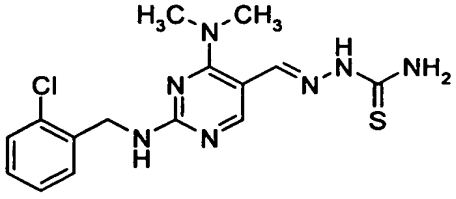
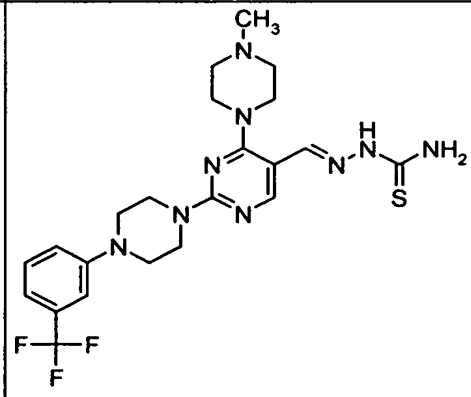
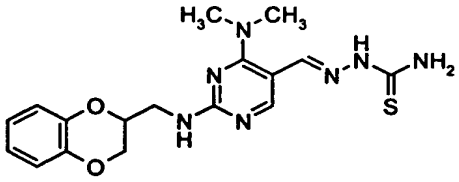
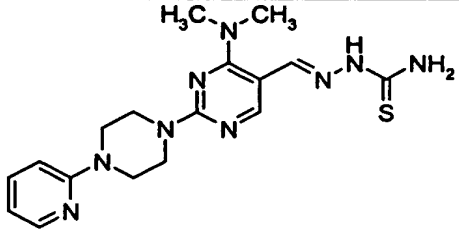
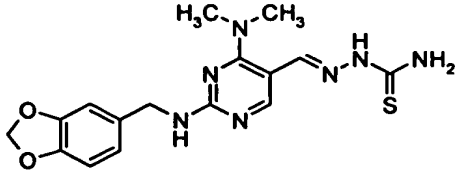
	Structure	Name	MH+
130		4-(dimethylamino)-2-[4-(4-methoxyphenyl)-3-methylpiperazin-1-yl]pyrimidine-5-carbaldehyde thiosemicarbazone	430
131		2-[(2-chlorobenzyl)amino]-4-(dimethylamino)pyrimidine-5-carbaldehyde thiosemicarbazone	365
132		4-(4-methylpiperazin-1-yl)-2-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}pyrimidine-5-carbaldehyde thiosemicarbazone	509
133		2-[(2,3-dihydro-1,4-benzodioxin-2-ylmethyl)amino]-4-(dimethylamino)pyrimidine-5-carbaldehyde thiosemicarbazone	388
134		4-(dimethylamino)-2-(4-pyridin-2-ylpiperazin-1-yl)pyrimidine-5-carbaldehyde thiosemicarbazone	386
135		2-[(1,3-benzodioxol-5-ylmethyl)amino]-4-(dimethylamino)pyrimidine-5-carbaldehyde thiosemicarbazone	374

TABLE 3

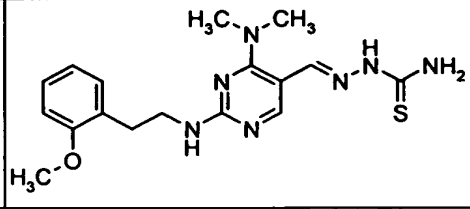
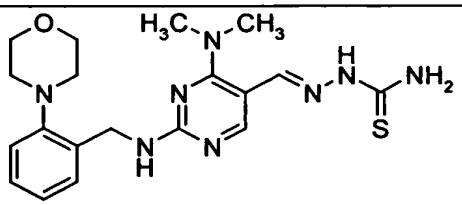
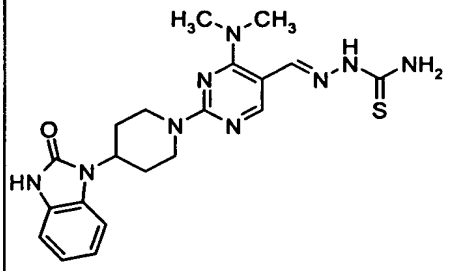
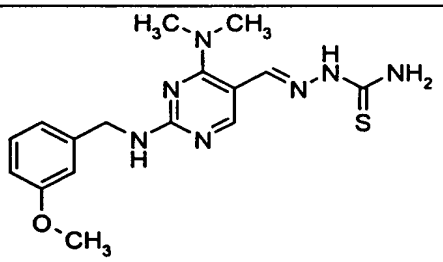
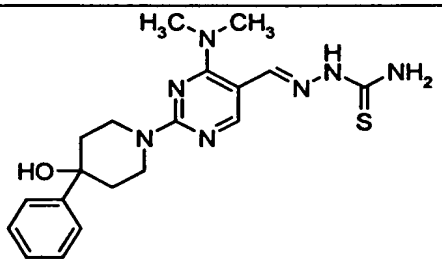
	Structure	Name	MH+
136		4-(dimethylamino)-2-{[2-(2-methoxyphenyl)ethyl]amino}pyrimidine-5-carbaldehyde thiosemicarbazone	374
137		4-(dimethylamino)-2-[(2-morpholin-4-ylbenzyl)amino]pyrimidine-5-carbaldehyde thiosemicarbazone	416
138		4-(dimethylamino)-2-[4-(2-oxo-2,3-dihydro-1H-benzimidazol-1-yl)piperidin-1-yl]pyrimidine-5-carbaldehyde thiosemicarbazone	441
139		4-(dimethylamino)-2-[(3-methoxybenzyl)amino]pyrimidine-5-carbaldehyde thiosemicarbazone	360
140		4-(dimethylamino)-2-(4-hydroxy-4-phenylpiperidin-1-yl)pyrimidine-5-carbaldehyde thiosemicarbazone	401

TABLE 3

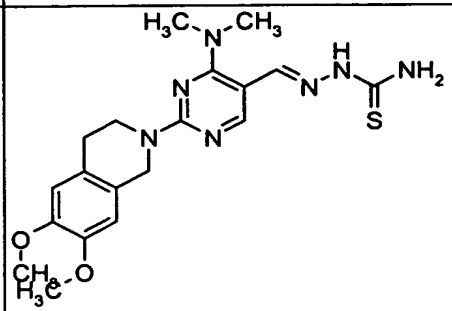
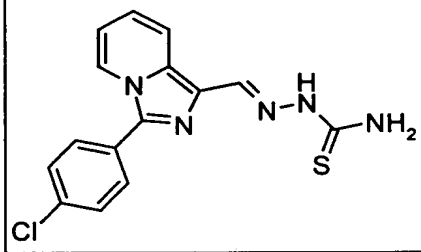
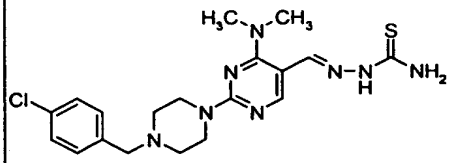
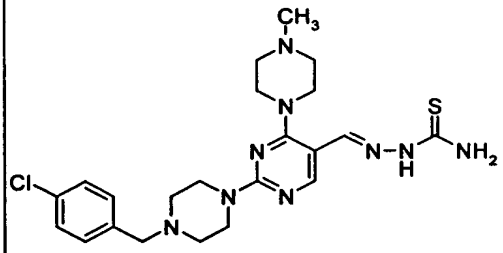
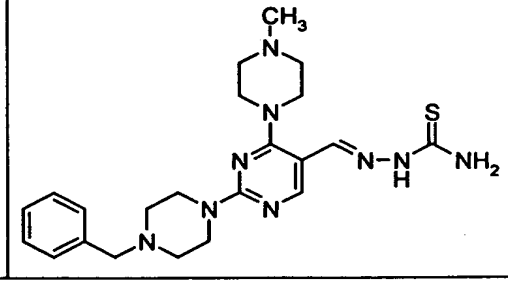
	Structure	Name	MH+
141		2-(6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)-4-(dimethylamino)pyrimidine-5-carbaldehyde thiosemicarbazone	417
142		3-(4-chlorophenyl)imidazo[1,5-a]pyridine-1-carbaldehyde thiosemicarbazone	331
143		2-[4-(4-chlorobenzyl)piperazin-1-yl]-4-(dimethylamino)pyrimidine-5-carbaldehyde thiosemicarbazone	434
144		2-[4-(4-chlorobenzyl)piperazin-1-yl]-4-(4-methylpiperazin-1-yl)pyrimidine-5-carbaldehyde thiosemicarbazone	489
145		2-(4-benzylpiperazin-1-yl)-4-(4-methylpiperazin-1-yl)pyrimidine-5-carbaldehyde thiosemicarbazone	455

TABLE 3

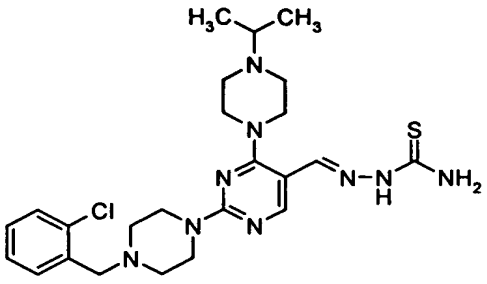
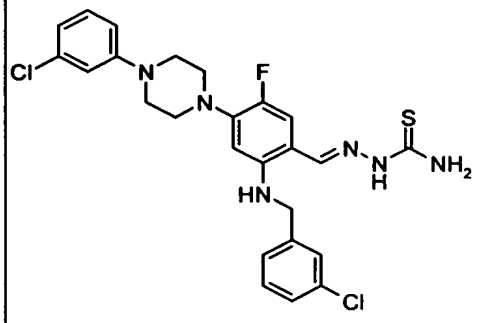
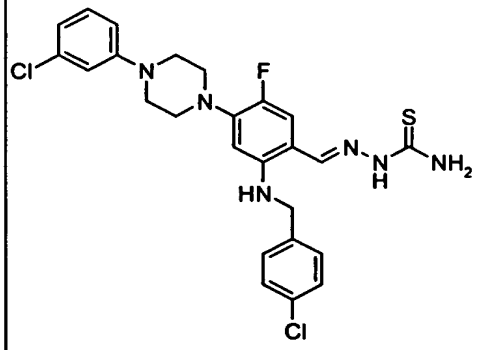
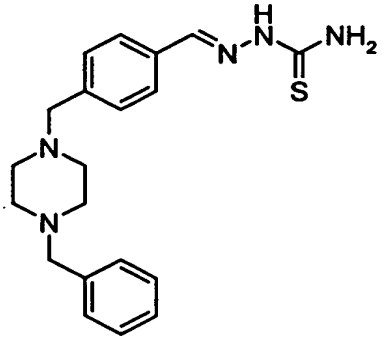
	Structure	Name	MH+
146		2-[4-(2-chlorobenzyl)piperazin-1-yl]-4-(4-isopropylpiperazin-1-yl)pyrimidine-5-carbaldehyde thiosemicarbazone	517
147		2-[(3-chlorobenzyl)amino]-4-[4-(3-chlorophenyl)piperazin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	532
148		2-[(4-chlorobenzyl)amino]-4-[4-(3-chlorophenyl)piperazin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	532
149		4-[(4-benzylpiperazin-1-yl)methyl]benzaldehyde thiosemicarbazone	369

TABLE 3

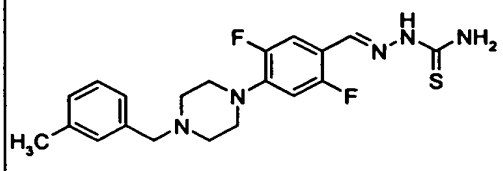
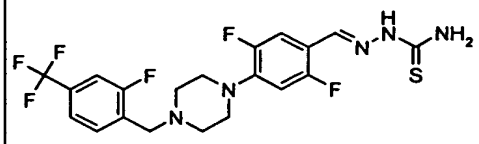
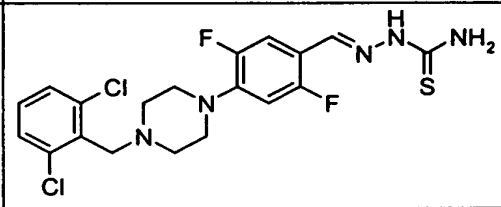
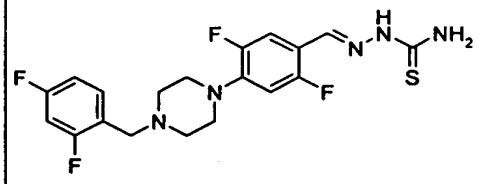
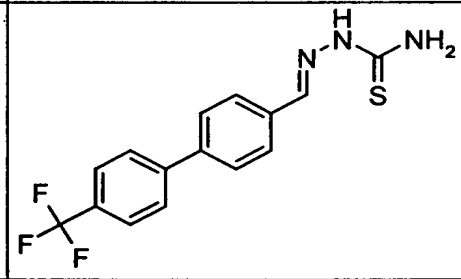
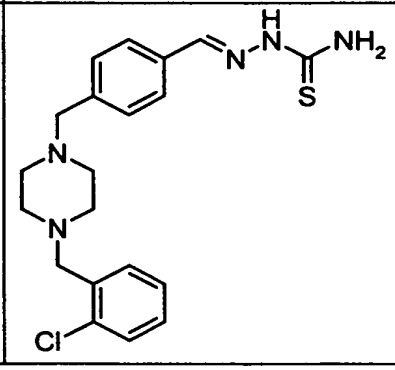
	Structure	Name	MH+
150		2,5-difluoro-4-[4-(3-methylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404
151		2,5-difluoro-4-{4-[2-fluoro-4-(trifluoromethyl)benzyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	476
152		4-[4-(2,6-dichlorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	459
153		4-[4-(2,4-difluorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	426
154		4'-(trifluoromethyl)-1,1'-biphenyl-4-carbaldehyde thiosemicarbazone	324
155		4-{[4-(2-chlorobenzyl)piperazin-1-yl]methyl}benzaldehyde thiosemicarbazone	403

TABLE 3

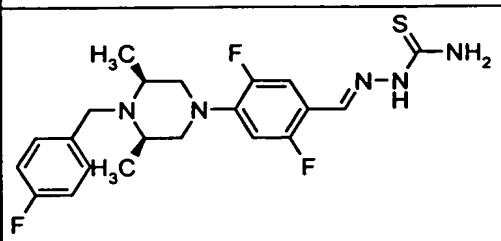
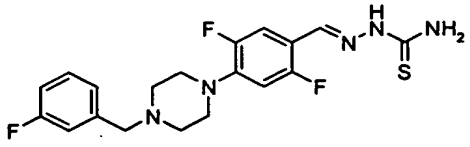
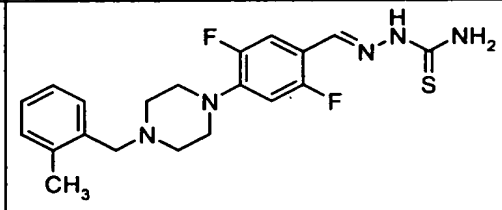
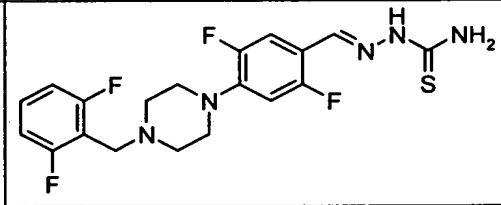
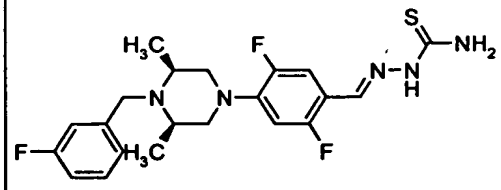
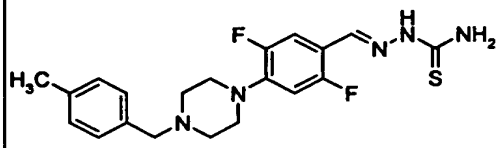
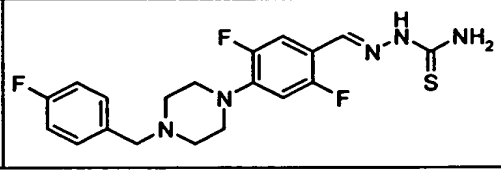
	Structure	Name	MH+
156		2,5-difluoro-4-[(3R,5S)-4-(4-fluorobenzyl)-3,5-dimethylpiperazin-1-yl]benzaldehyde thiosemicarbazone	437
157		2,5-difluoro-4-[4-(3-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	408
158		2,5-difluoro-4-[4-(2-methylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404
159		4-[4-(2,6-difluorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	426
160		2,5-difluoro-4-[(3R,5S)-4-(3-fluorobenzyl)-3,5-dimethylpiperazin-1-yl]benzaldehyde thiosemicarbazone	437
161		2,5-difluoro-4-[4-(4-methylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404
162		2,5-difluoro-4-[4-(4-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	408

TABLE 3

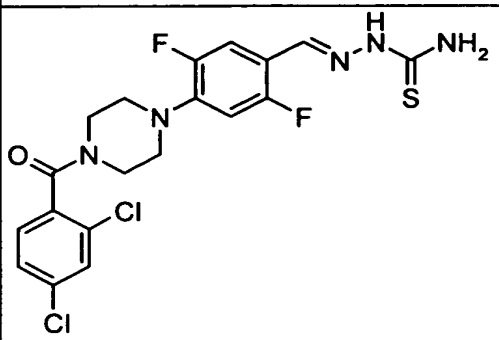
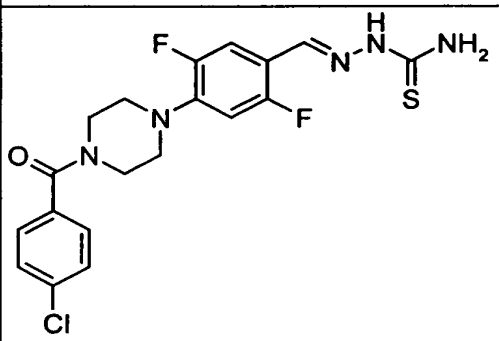
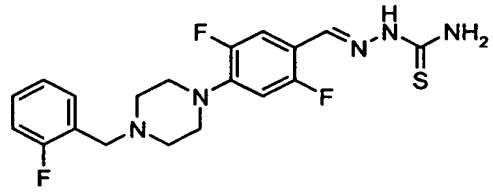
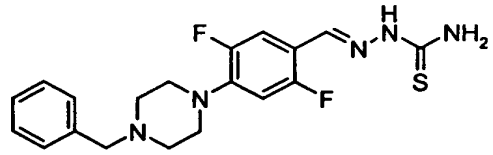
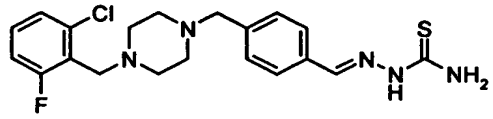
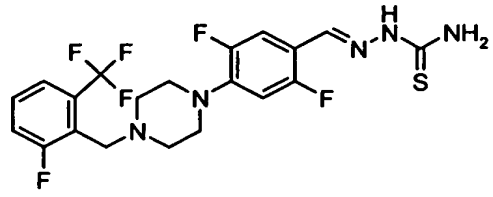
	Structure	Nam	MH+
163		4-[4-(2,4-dichlorobenzoyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	473
164		4-[4-(4-chlorobenzoyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	439
165		2,5-difluoro-4-[4-(2-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	408
166		4-(4-benzylpiperazin-1-yl)-2,5-difluorobenzaldehyde thiosemicarbazone	390
167		4-{[4-(2-chloro-6-fluorobenzyl)piperazin-1-yl]methyl}benzaldehyde thiosemicarbazone	421
168		2,5-difluoro-4-{4-[2-fluoro-6-(trifluoromethyl)benzyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	476

TABLE 3

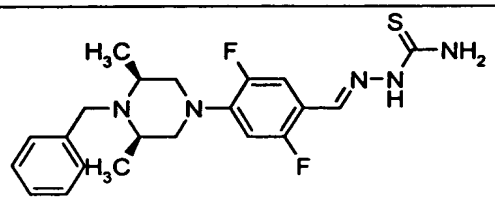
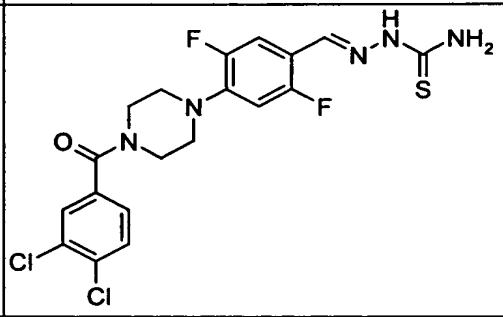
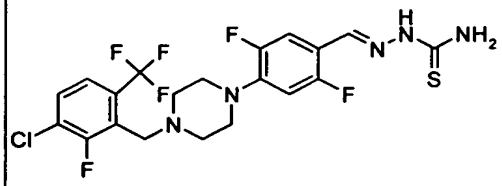
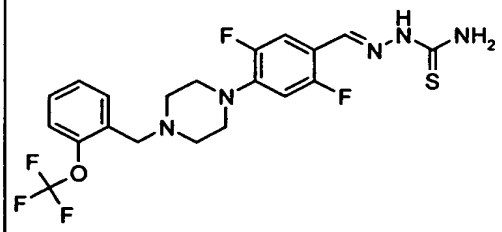
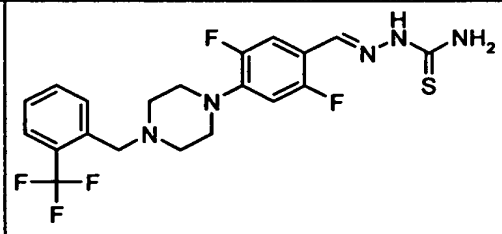
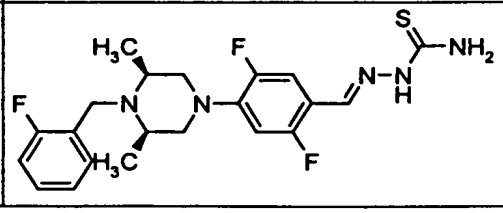
	Structur	Name	MH+
169		4-[(3R,5S)-4-benzyl-3,5-dimethylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	419
170		4-[4-(3,4-dichlorobenzoyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	473
171		4-{4-[3-chloro-2-fluoro-6-(trifluoromethyl)benzyl]piperazin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	511
172		2,5-difluoro-4-{4-[2-(trifluoromethoxy)benzyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	474
173		2,5-difluoro-4-{4-[2-(trifluoromethyl)benzyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	458
174		2,5-difluoro-4-[(3R,5S)-4-(2-fluorobenzyl)-3,5-dimethylpiperazin-1-yl]benzaldehyde thiosemicarbazone	437

TABLE 3

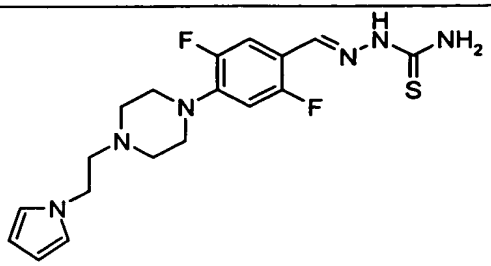
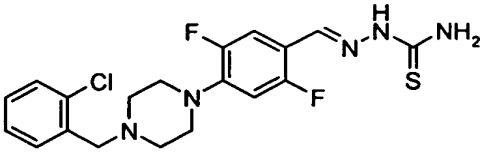
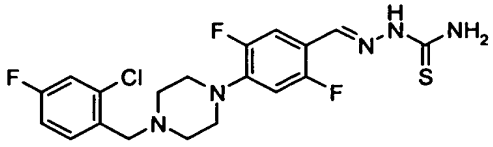
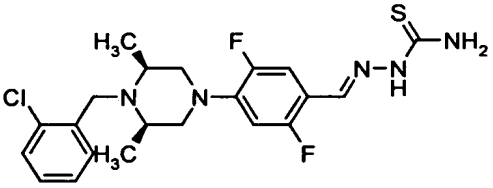
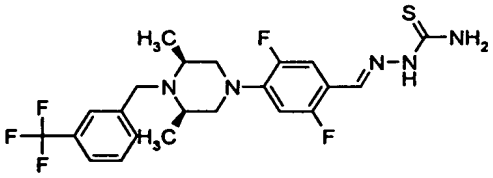
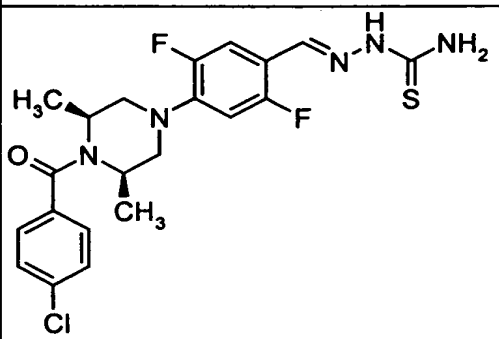
	Structure	Name	MH+
175		2,5-difluoro-4-{4-[2-(1H-pyrrol-1-yl)ethyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	393
176		4-[4-(2-chlorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	425
177		4-[4-(2-chloro-4-fluorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	443
178		4-[(3R,5S)-4-(2-chlorobenzyl)-3,5-dimethylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	453
179		4-{(3R,5S)-3,5-dimethyl-4-[3-(trifluoromethyl)benzyl]piperazin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	487
180		4-[(3R,5S)-4-(4-chlorobenzoyl)-3,5-dimethylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	467

TABLE 3

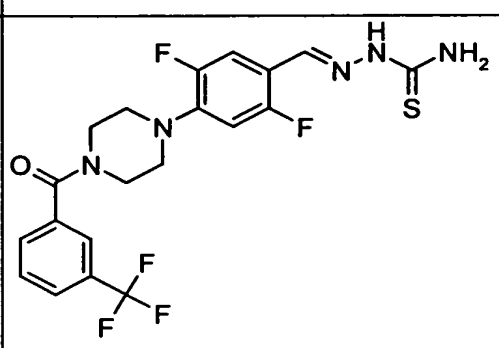
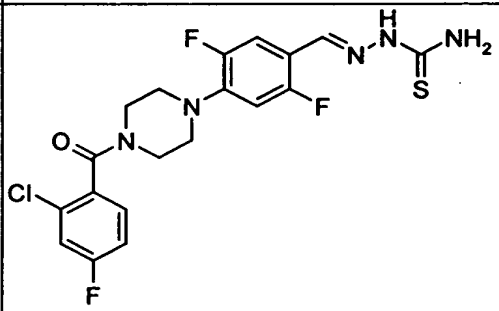
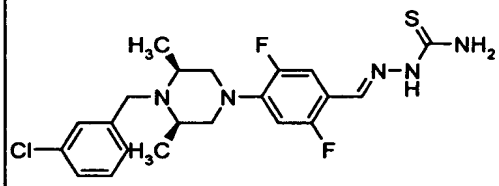
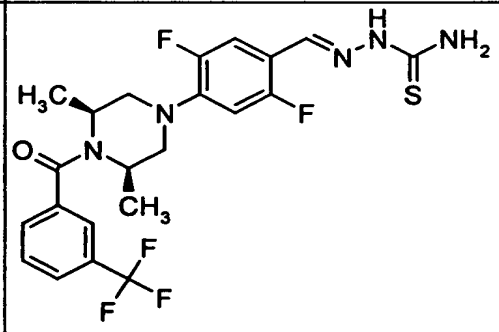
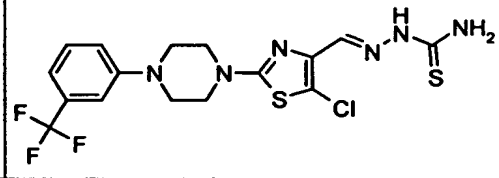
	Structure	Name	MH+
181		2,5-difluoro-4-{4-[3-(trifluoromethyl)benzoyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	472
182		4-[4-(2-chloro-4-fluorobenzoyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	457
183		4-[(3R,5S)-4-(3-chlorobenzyl)-3,5-dimethylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	453
184		4-{(3R,5S)-3,5-dimethyl-4-[3-(trifluoromethyl)benzoyl]piperazin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	501
185		5-chloro-2-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}-1,3-thiazole-4-carbaldehyde thiosemicarbazone	450

TABLE 3

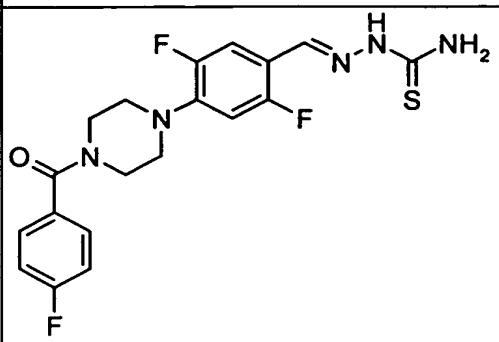
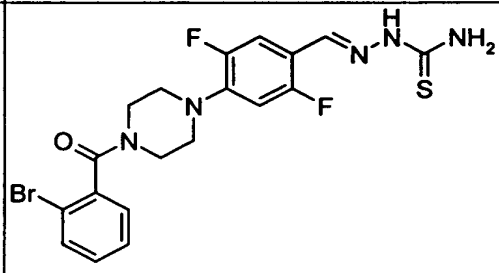
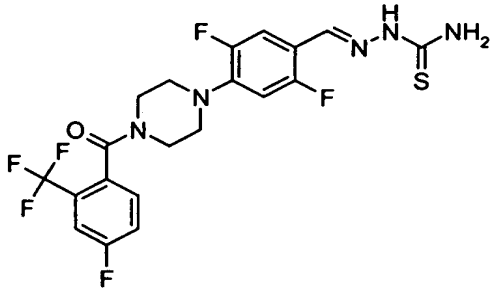
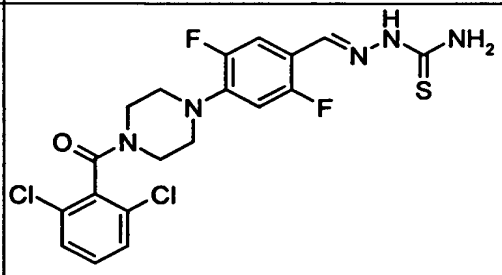
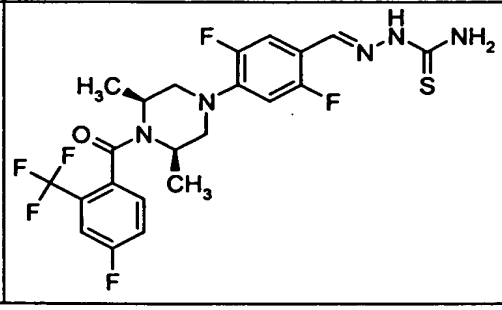
	Structure	Name	MH+
186		2,5-difluoro-4-[4-(4-fluorobenzoyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	422
187		4-[4-(2-bromobenzoyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	483
188		2,5-difluoro-4-{4-[4-fluoro-2-(trifluoromethyl)benzoyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	490
189		4-[4-(2,6-dichlorobenzoyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	473
190		2,5-difluoro-4-{(3R,5S)-4-[4-fluoro-2-(trifluoromethyl)benzoyl]-3,5-dimethylpiperazin-1-yl}benzaldehyde thiosemicarbazone	518

TABLE 3

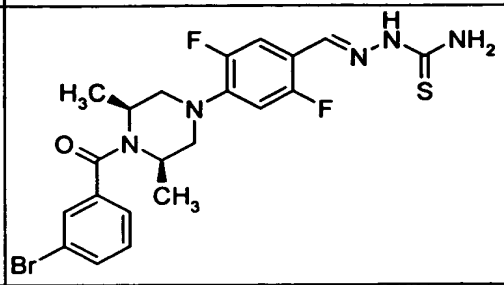
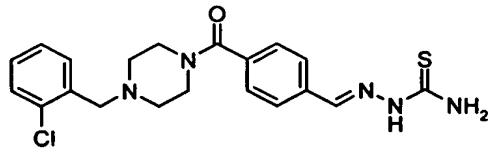
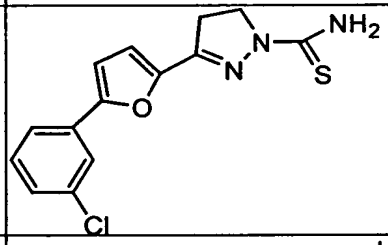
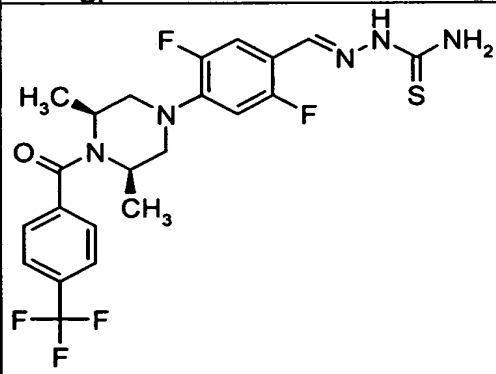
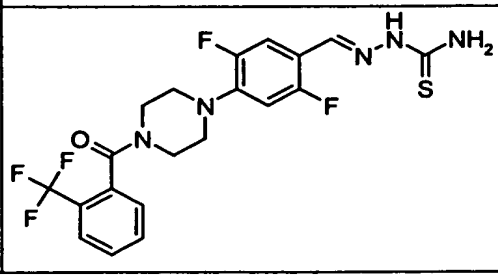
	Structure	Name	MH+
191		4-[(3R,5S)-4-(3-bromobenzoyl)-3,5-dimethylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	511
192		4-{[4-(2-chlorobenzyl)piperazin-1-yl]carbonyl}benzaldehyde thiosemicarbazone	417
193		3-[5-(3-chlorophenyl)-2-furyl]-4,5-dihydro-1H-pyrazole-1-carbothioamide	307
194		4-{(3R,5S)-3,5-dimethyl-4-[4-(trifluoromethyl)benzoyl]piperazin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	501
195		2,5-difluoro-4-{4-[2-(trifluoromethyl)benzoyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	472

TABLE 3

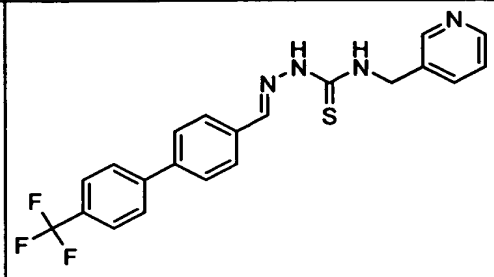
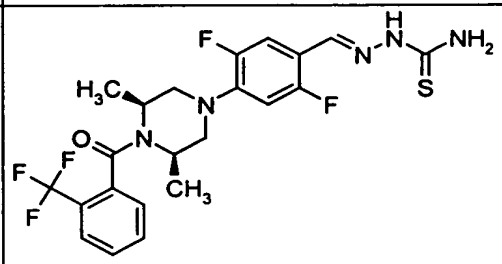
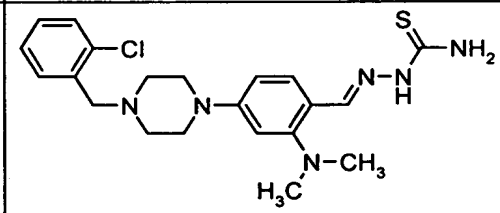
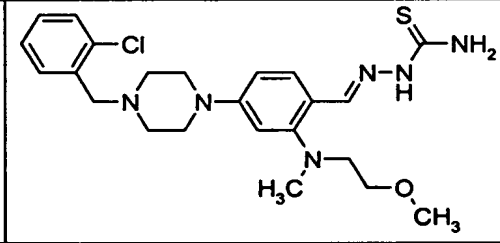
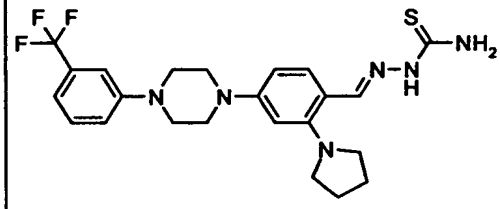
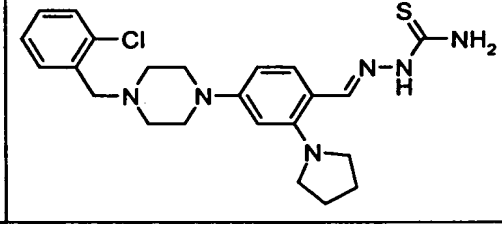
	Structure	Name	MH+
196		4'-(trifluoromethyl)-1,1'-biphenyl-4-carbaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone	415
197		4-{(3R,5S)-3,5-dimethyl-4-[2-(trifluoromethyl)benzoyl]piperazin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	501
198		4-[4-(2-chlorobenzyl)piperazin-1-yl]-2-(dimethylamino)benzaldehyde thiosemicarbazone	432
199		4-[4-(2-chlorobenzyl)piperazin-1-yl]-2-[(2-methoxyethyl)(methyl)amino]benzaldehyde thiosemicarbazone	476
200		2-pyrrolidin-1-yl-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	478
201		4-[4-(2-chlorobenzyl)piperazin-1-yl]-2-pyrrolidin-1-ylbenzaldehyde thiosemicarbazone	458

TABLE 3

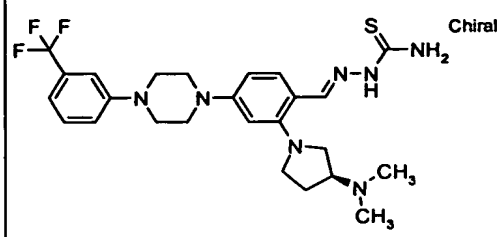
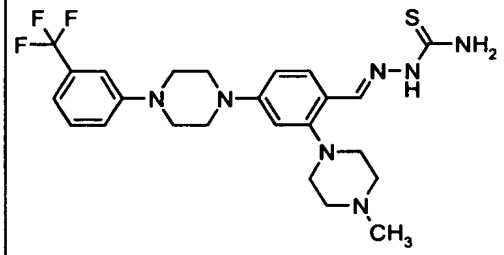
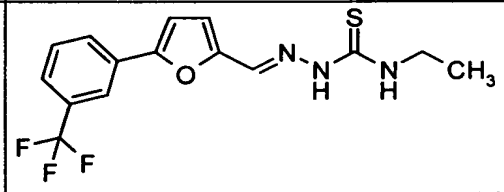
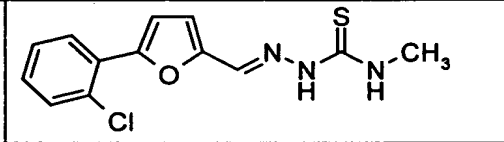
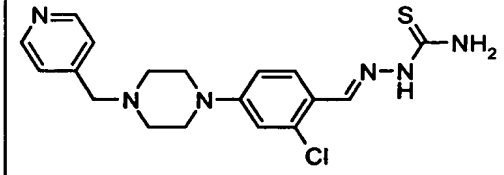
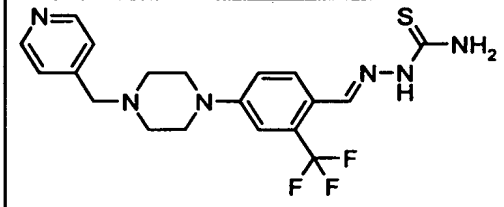
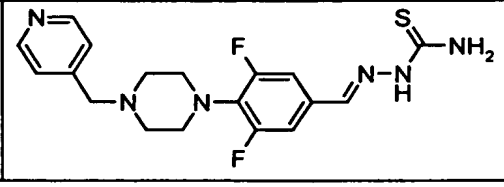
	Structure	Name	MH+
202		2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	521
203		2-(4-methylpiperazin-1-yl)-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	507
204		5-[3-(trifluoromethyl)phenyl]-2-furaldehyde N-ethylthiosemicarbazone	342
205		5-(2-chlorophenyl)-2-furaldehyde N-methylthiosemicarbazone	295
206		2-chloro-4-[4-(pyridin-4-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	390
207		4-[4-(pyridin-4-ylmethyl)piperazin-1-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	423
208		3,5-difluoro-4-[4-(pyridin-4-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	391

TABLE 3

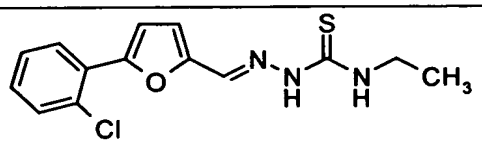
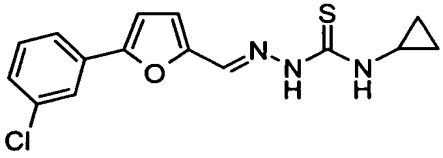
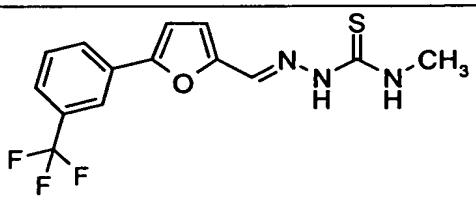
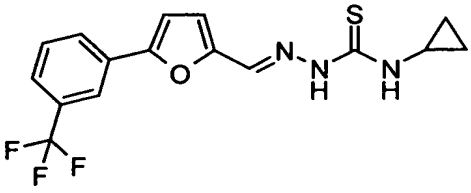
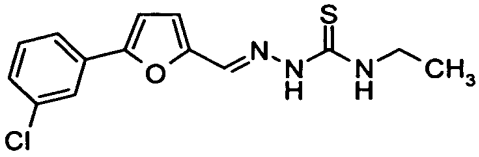
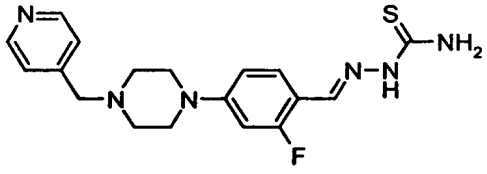
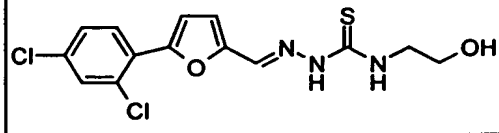
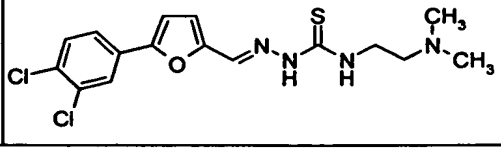
	Structure	Name	MH+
209		5-(2-chlorophenyl)-2-furaldehyde N-ethylthiosemicarbazone	309
210		5-(3-chlorophenyl)-2-furaldehyde N-cyclopropylthiosemicarbazone	321
211		5-[3-(trifluoromethyl)phenyl]-2-furaldehyde N-methylthiosemicarbazone	328
212		5-[3-(trifluoromethyl)phenyl]-2-furaldehyde N-cyclopropylthiosemicarbazone	354
213		5-(3-chlorophenyl)-2-furaldehyde N-ethylthiosemicarbazone	309
214		2-fluoro-4-[4-(pyridin-4-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	373
215		5-(2,4-dichlorophenyl)-2-furaldehyde N-(2-hydroxyethyl)thiosemicarbazone	359
216		5-(3,4-dichlorophenyl)-2-furaldehyde N-[2-(dimethylamino)ethyl]thiosemicarbazone	386

TABLE 3

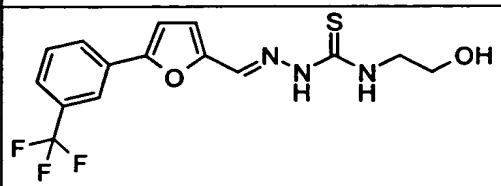
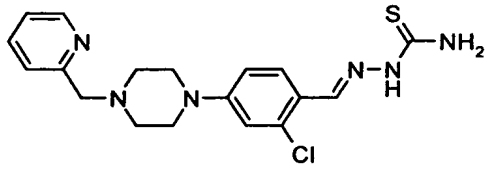
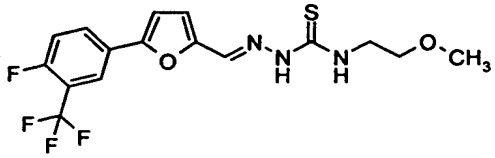
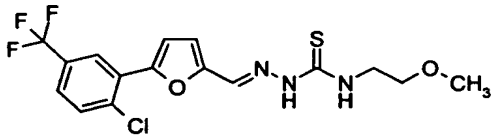
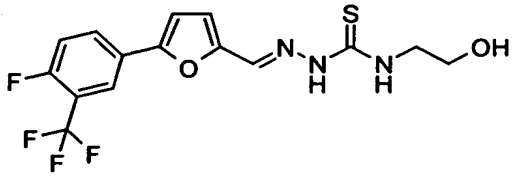
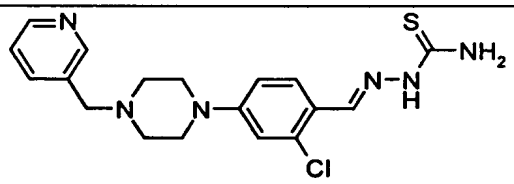
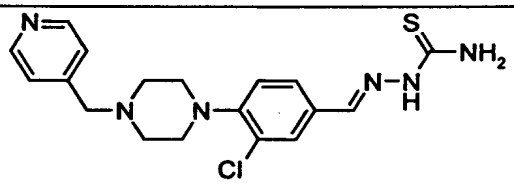
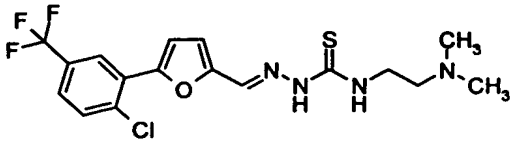
	Structure	Nam	MH+
217		5-[3-(trifluoromethyl)phenyl]-2-furaldehyde N-(2-hydroxyethyl)thiosemicarbazone	358
218		2-chloro-4-[4-(pyridin-2-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	390
219		5-[4-fluoro-3-(trifluoromethyl)phenyl]-2-furaldehyde N-(2-methoxyethyl)thiosemicarbazone	390
220		5-[2-chloro-5-(trifluoromethyl)phenyl]-2-furaldehyde N-(2-methoxyethyl)thiosemicarbazone	407
221		5-[4-fluoro-3-(trifluoromethyl)phenyl]-2-furaldehyde N-(2-hydroxyethyl)thiosemicarbazone	376
222		2-chloro-4-[4-(pyridin-3-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	390
223		3-chloro-4-[4-(pyridin-4-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	390
224		5-[2-chloro-5-(trifluoromethyl)phenyl]-2-furaldehyde N-[2-(dimethylamino)ethyl]thiosemicarbazone	420

TABLE 3

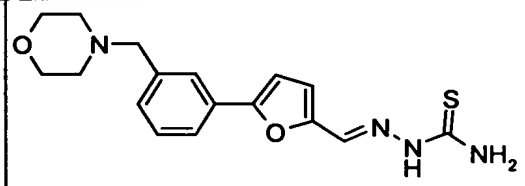
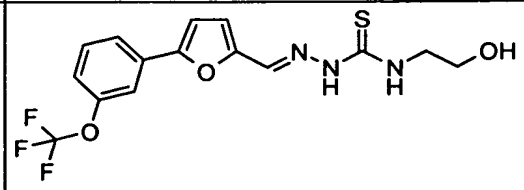
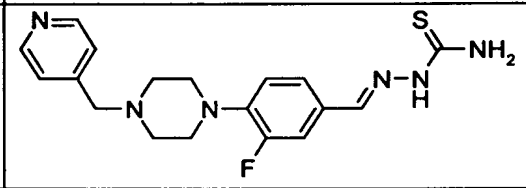
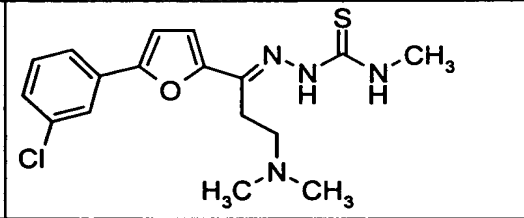
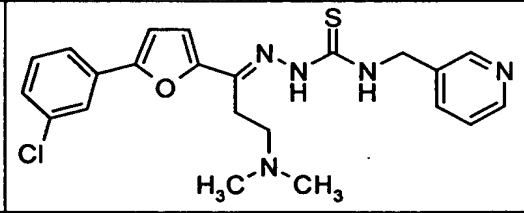
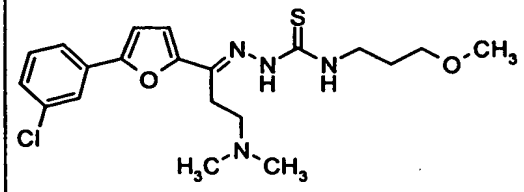
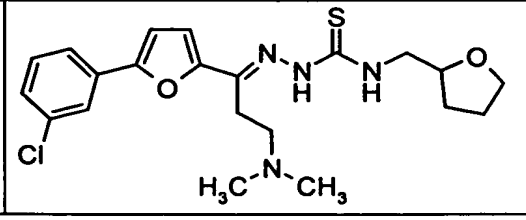
	Structur	Name	MH+
225		5-[3-(morpholin-4-ylmethyl)phenyl]-2-furaldehyde thiosemicarbazone	345
226		5-[3-(trifluoromethoxy)phenyl]-2-furaldehyde N-(2-hydroxyethyl)thiosemicarbazone	374
227		3-fluoro-4-[4-(pyridin-4-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	373
228		(1E)-1-[5-(3-chlorophenyl)-2-furyl]-3-(dimethylamino)propan-1-one N-methylthiosemicarbazone	366
229		(1E)-1-[5-(3-chlorophenyl)-2-furyl]-3-(dimethylamino)propan-1-one N-(pyridin-3-ylmethyl)thiosemicarbazone	443
230		(1E)-1-[5-(3-chlorophenyl)-2-furyl]-3-(dimethylamino)propan-1-one N-(3-methoxypropyl)thiosemicarbazone	424
231		(1E)-1-[5-(3-chlorophenyl)-2-furyl]-3-(dimethylamino)propan-1-one N-(tetrahydrofuran-2-ylmethyl)thiosemicarbazone	436

TABLE 3

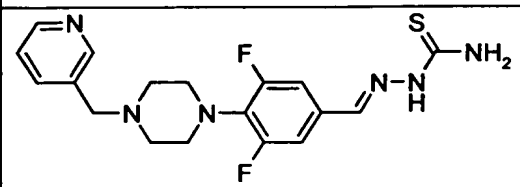
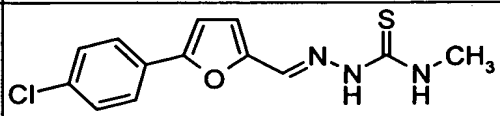
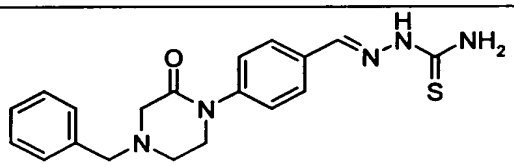
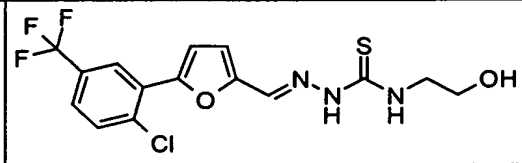
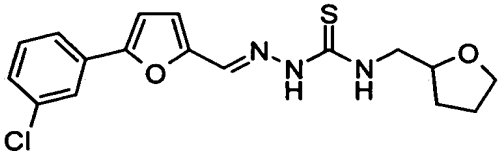
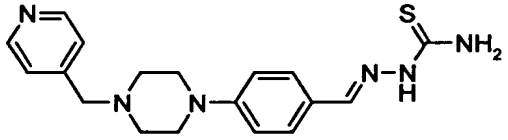
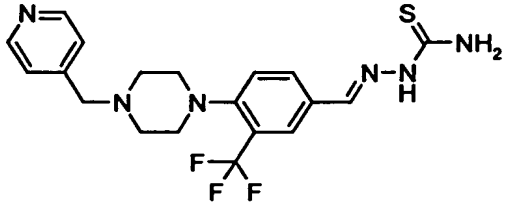
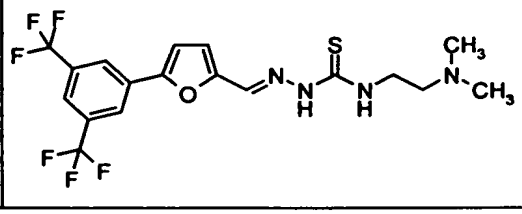
	Structure	Name	MH+
232		3,5-difluoro-4-[4-(pyridin-3-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	391
233		5-(4-chlorophenyl)-2-furaldehyde N-methylthiosemicarbazone	295
234		4-(4-benzyl-2-oxopiperazin-1-yl)benzaldehyde thiosemicarbazone	368
235		5-[2-chloro-5-(trifluoromethyl)phenyl]-2-furaldehyde N-(2-hydroxyethyl)thiosemicarbazone	393
236		5-(3-chlorophenyl)-2-furaldehyde N-(tetrahydrofuran-2-ylmethyl)thiosemicarbazone	365
237		4-[4-(pyridin-4-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	355
238		4-[4-(pyridin-4-ylmethyl)piperazin-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	423
239		5-[3,5-bis(trifluoromethyl)phenyl]-2-furaldehyde N-[2-(dimethylamino)ethyl]thiosemicarbazone	453

TABLE 3

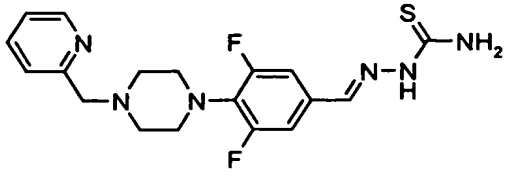
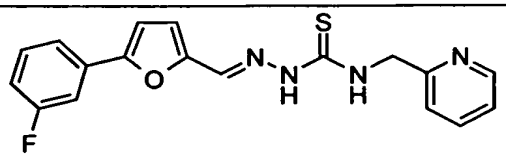
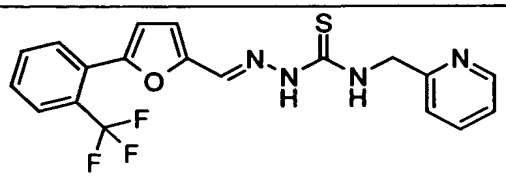
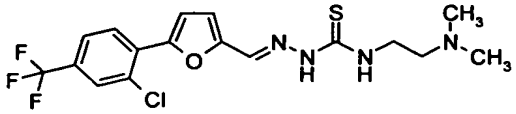
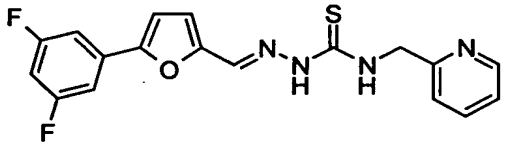
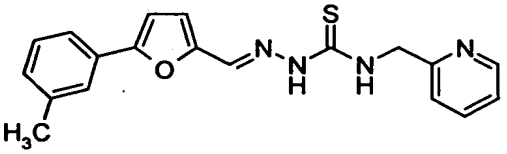
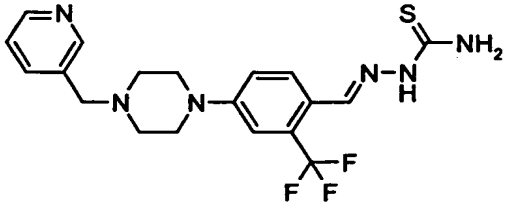
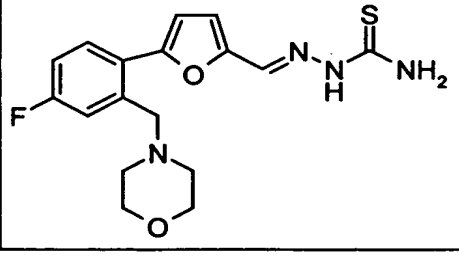
	Structure	Name	MH+
240		3,5-difluoro-4-[4-(pyridin-2-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	391
241		5-(3-fluorophenyl)-2-furaldehyde N-(pyridin-2-ylmethyl)thiosemicarbazone	355
242		5-[2-(trifluoromethyl)phenyl]-2-furaldehyde N-(pyridin-2-ylmethyl)thiosemicarbazone	405
243		5-[2-chloro-4-(trifluoromethyl)phenyl]-2-furaldehyde N-[2-(dimethylamino)ethyl]thiosemicarbazone	420
244		5-(3,5-difluorophenyl)-2-furaldehyde N-(pyridin-2-ylmethyl)thiosemicarbazone	373
245		5-(3-methylphenyl)-2-furaldehyde N-(pyridin-2-ylmethyl)thiosemicarbazone	351
246		4-[4-(pyridin-3-ylmethyl)piperazin-1-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	423
247		5-[4-fluoro-2-(morpholin-4-ylmethyl)phenyl]-2-furaldehyde thiosemicarbazone	363

TABLE 3

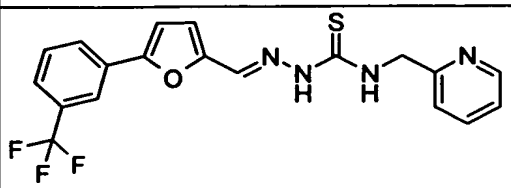
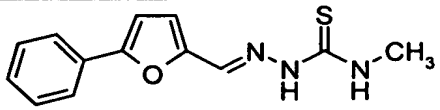
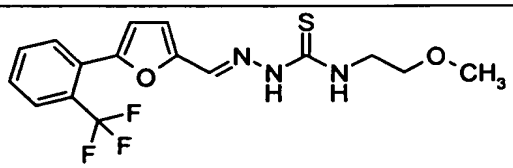
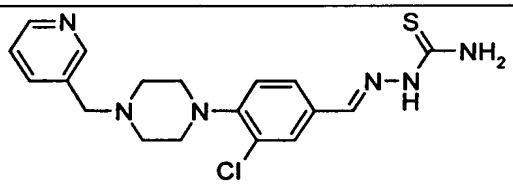
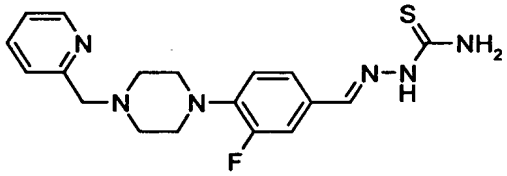
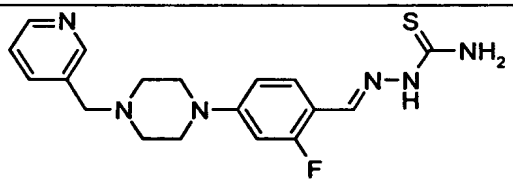
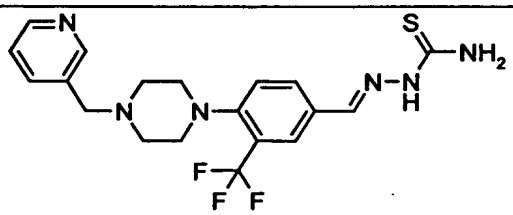
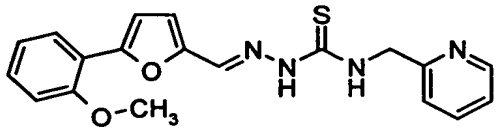
	Structure	Name	MH+
248		5-[3-(trifluoromethyl)phenyl]-2-furaldehyde N-(pyridin-2-ylmethyl)thiosemicarbazone	405
249		5-phenyl-2-furaldehyde N-methylthiosemicarbazone	260
250		5-[2-(trifluoromethyl)phenyl]-2-furaldehyde N-(2-methoxyethyl)thiosemicarbazone	372
251		3-chloro-4-[4-(pyridin-3-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	390
252		3-fluoro-4-[4-(pyridin-2-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	373
253		2-fluoro-4-[4-(pyridin-3-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	373
254		4-[4-(pyridin-3-ylmethyl)piperazin-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	423
255		5-(2-methoxyphenyl)-2-furaldehyde N-(pyridin-2-ylmethyl)thiosemicarbazone	367

TABLE 3

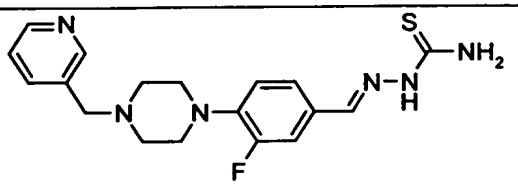
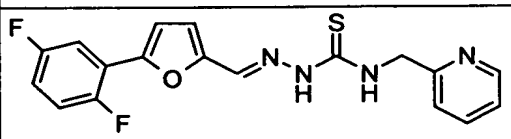
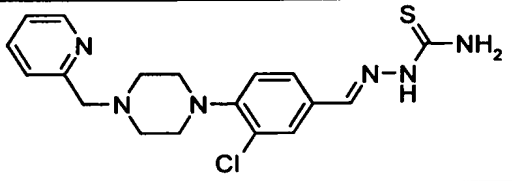
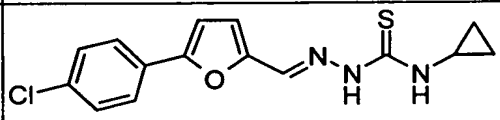
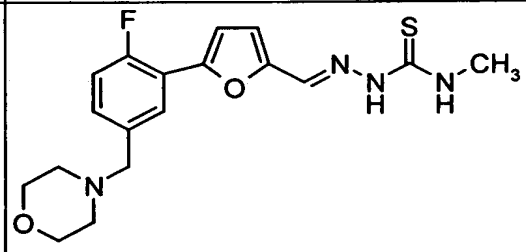
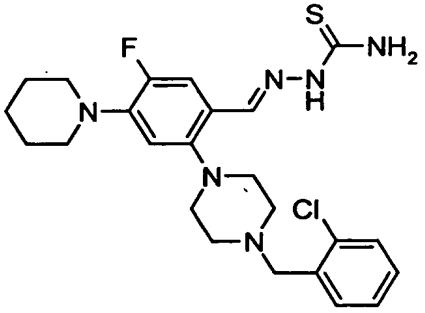
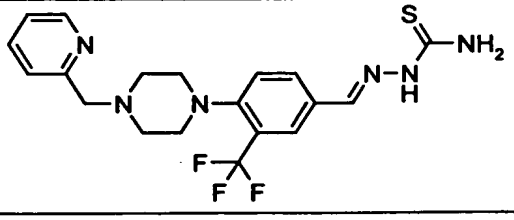
	Structure	Name	MH+
256		3-fluoro-4-[4-(pyridin-3-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	373
257		5-(2,5-difluorophenyl)-2-furaldehyde N-(pyridin-2-ylmethyl)thiosemicarbazone	373
258		3-chloro-4-[4-(pyridin-2-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	390
259		5-(4-chlorophenyl)-2-furaldehyde N-cyclopropylthiosemicarbazone	321
260		5-[2-fluoro-5-(morpholin-4-ylmethyl)phenyl]-2-furaldehyde N-methylthiosemicarbazone	377
261		2-[4-(2-chlorobenzyl)piperazin-1-yl]-5-fluoro-4-piperidin-1-ylbenzaldehyde thiosemicarbazone	490
262		4-[4-(pyridin-2-ylmethyl)piperazin-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	423

TABLE 3

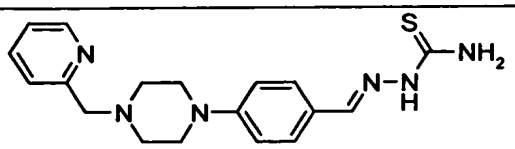
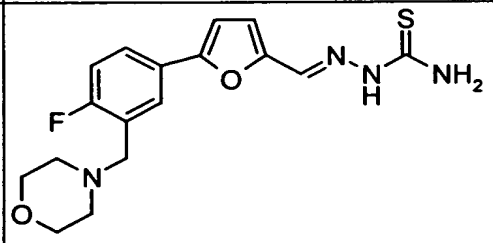
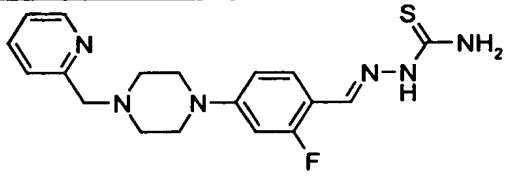
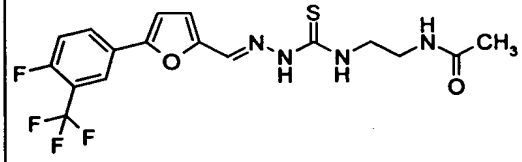
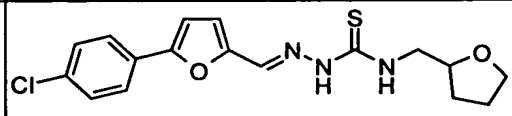
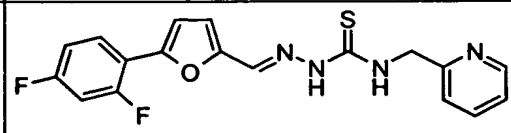
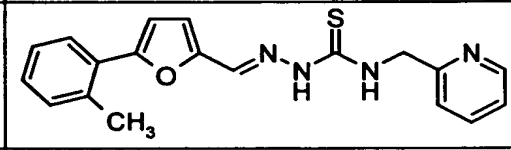
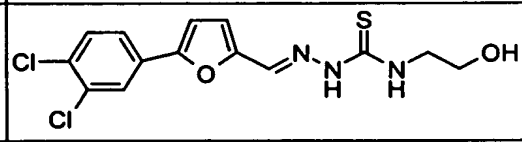
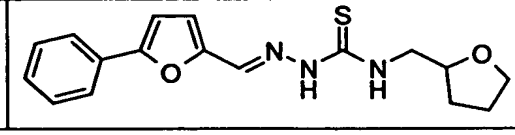
	Structure	Name	MH+
263		4-[4-(pyridin-2-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	355
264		5-[4-fluoro-3-(morpholin-4-ylmethyl)phenyl]-2-furaldehyde thiosemicarbazone	363
265		2-fluoro-4-[4-(pyridin-2-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	373
266		N-[2-({[(2E)-2-({5-[4-fluoro-3-(trifluoromethyl)phenyl]-2-furyl}methylene)hydrazino]carbonothioyl}amino)ethyl]acetamide	417
267		5-(4-chlorophenyl)-2-furaldehyde N-(tetrahydrofuran-2-ylmethyl)thiosemicarbazone	365
268		5-(2,4-difluorophenyl)-2-furaldehyde N-(pyridin-2-ylmethyl)thiosemicarbazone	373
269		5-(2-methylphenyl)-2-furaldehyde N-(pyridin-2-ylmethyl)thiosemicarbazone	351
270		5-(3,4-dichlorophenyl)-2-furaldehyde N-(2-hydroxyethyl)thiosemicarbazone	359
271		5-phenyl-2-furaldehyde N-(tetrahydrofuran-2-ylmethyl)thiosemicarbazone	330

TABLE 3

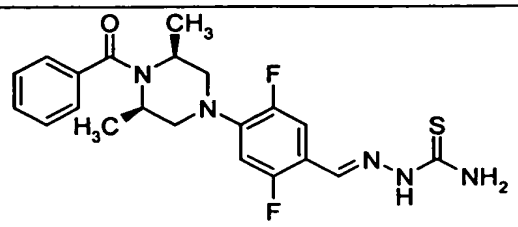
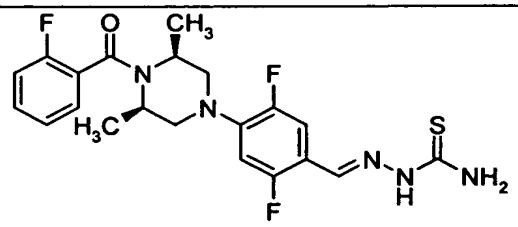
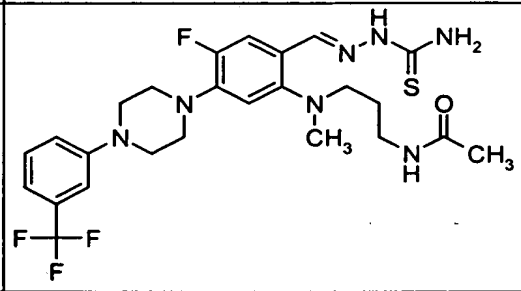
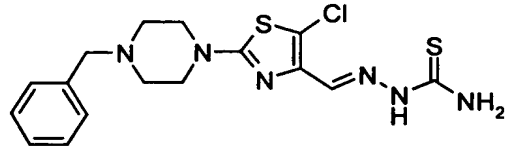
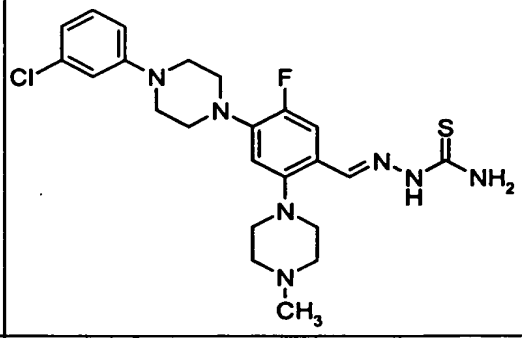
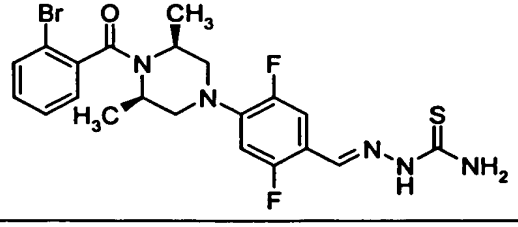
	Structur	Name	MH+
272		4-[(3R,5S)-4-benzoyl-3,5-dimethylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	433
273		2,5-difluoro-4-[(3R,5S)-4-(2-fluorobenzoyl)-3,5-dimethylpiperazin-1-yl]benzaldehyde thiosemicarbazone	450
274		N-{3-[(2-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-4-fluoro-5-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}phenyl)(methyl)amino]propyl}acetamide	555
275		2-(4-benzylpiperazin-1-yl)-5-chloro-1,3-thiazole-4-carbaldehyde thiosemicarbazone	396
276		4-[4-(3-chlorophenyl)piperazin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	491
277		4-[(3R,5S)-4-(2-bromobenzoyl)-3,5-dimethylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	511

TABLE 3

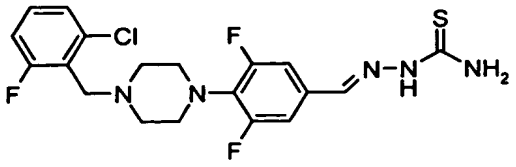
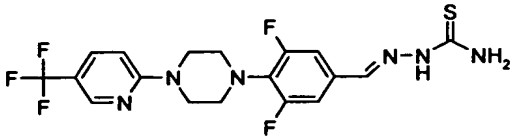
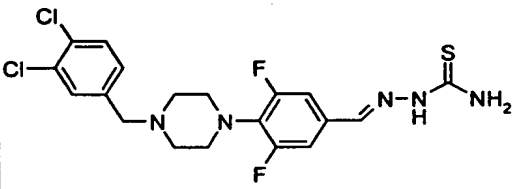
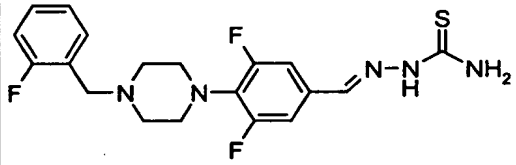
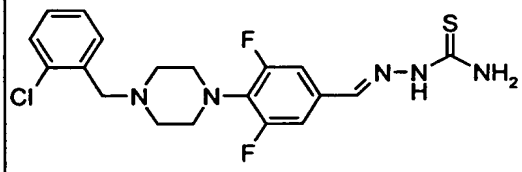
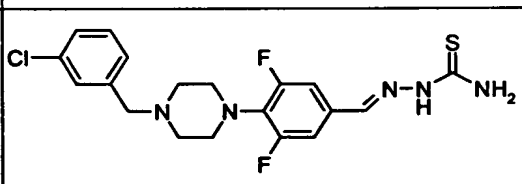
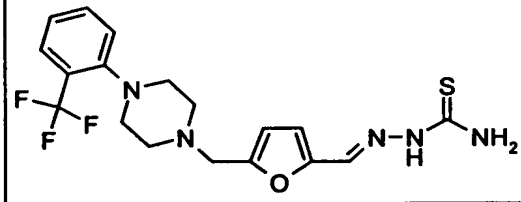
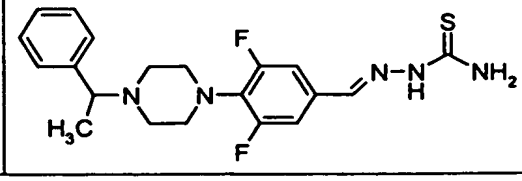
	Structure	Name	MH+
278		4-[4-(2-chloro-6-fluorobenzyl)piperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	443
279		3,5-difluoro-4-{4-[5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}benzaldehyde thiosemicarbazone	445
280		4-[4-(3,4-dichlorobenzyl)piperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	459
281		3,5-difluoro-4-[4-(2-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	408
282		4-[4-(2-chlorobenzyl)piperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	425
283		4-[4-(3-chlorobenzyl)piperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	425
284		5-({4-[2-(trifluoromethyl)phenyl]piperazin-1-yl}methyl)-2-furaldehyde thiosemicarbazone	412
285		3,5-difluoro-4-[4-(1-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404

TABLE 3

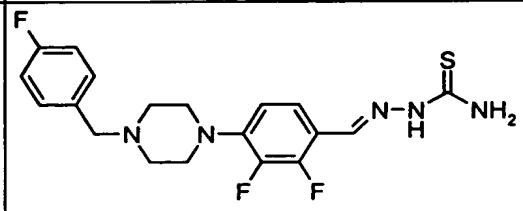
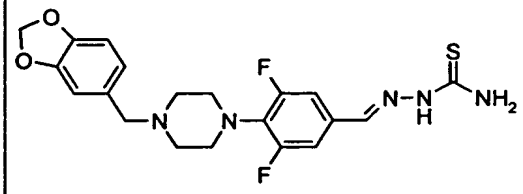
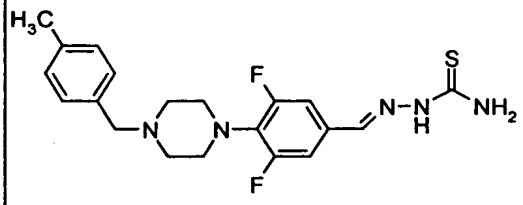
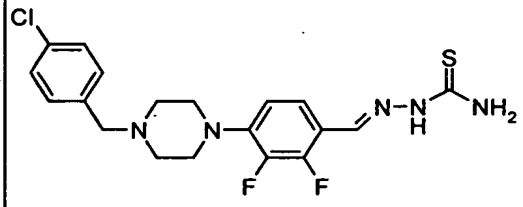
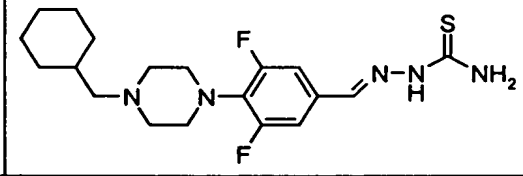
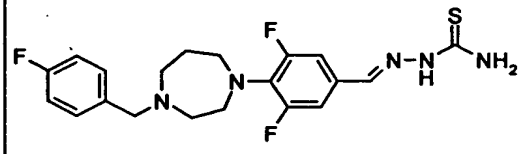
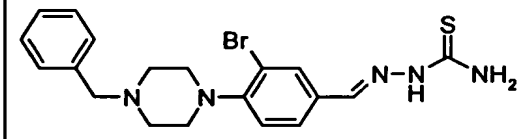
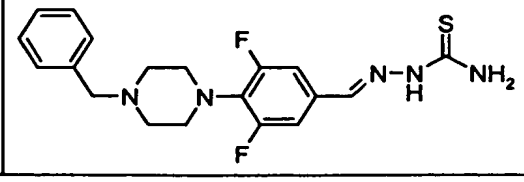
	Structure	Name	MH+
286		2,3-difluoro-4-[4-(4-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	408
287		4-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	434
288		3,5-difluoro-4-[4-(4-methylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404
289		4-[4-(4-chlorobenzyl)piperazin-1-yl]-2,3-difluorobenzaldehyde thiosemicarbazone	425
290		4-[4-(cyclohexylmethyl)piperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	397
291		3,5-difluoro-4-[4-(4-fluorobenzyl)-1,4-diazepan-1-yl]benzaldehyde thiosemicarbazone	422
292		4-(4-benzylpiperazin-1-yl)-3-bromobenzaldehyde thiosemicarbazone	433
293		4-(4-benzylpiperazin-1-yl)-3,5-difluorob nzaldehyde thiosemicarbazone	390

TABLE 3

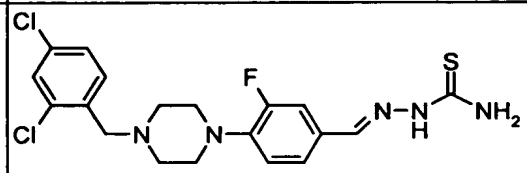
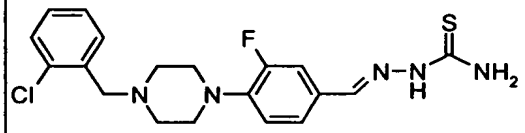
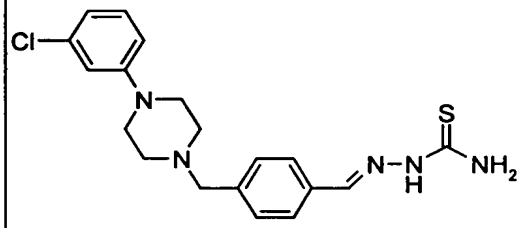
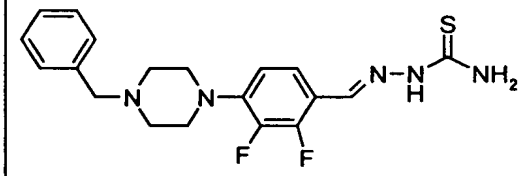
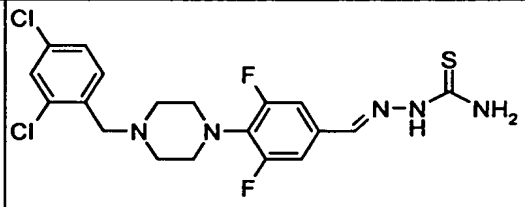
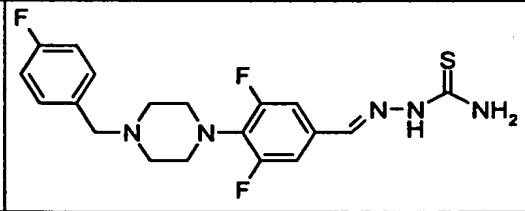
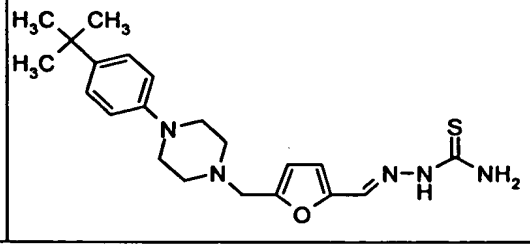
	Structure	Name	MH+
294		4-[4-(2,4-dichlorobenzyl)piperazin-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	441
295		4-[4-(2-chlorobenzyl)piperazin-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	407
296		4-{[4-(3-chlorophenyl)piperazin-1-yl]methyl}benzaldehyde thiosemicarbazone	389
297		4-(4-benzylpiperazin-1-yl)-2,3-difluorobenzaldehyde thiosemicarbazone	390
298		4-[4-(2,4-dichlorobenzyl)piperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	459
299		3,5-difluoro-4-[4-(4-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	408
300		5-{[4-(4-tert-butylphenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	401

TABLE 3

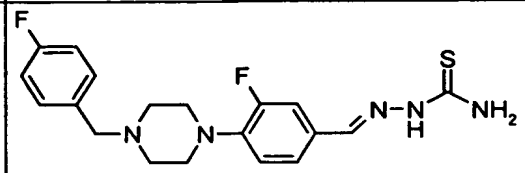
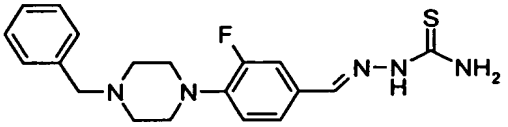
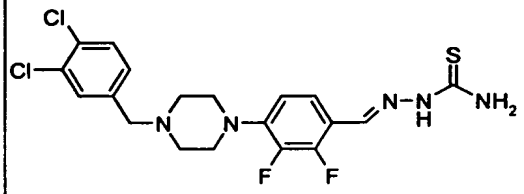
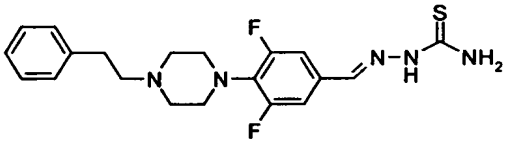
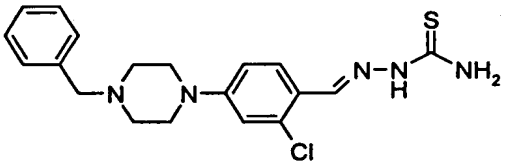
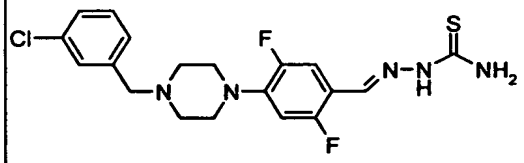
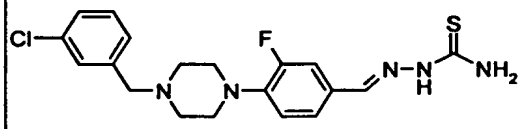
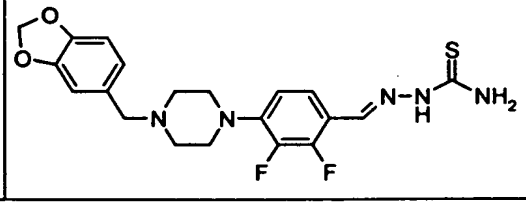
	Structure	Name	MH+
301		3-fluoro-4-[4-(4-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	390
302		4-(4-benzylpiperazin-1-yl)-3-fluorobenzaldehyde thiosemicarbazone	372
303		4-[4-(3,4-dichlorobenzyl)piperazin-1-yl]-2,3-difluorobenzaldehyde thiosemicarbazone	459
304		3,5-difluoro-4-[4-(2-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404
305		4-(4-benzylpiperazin-1-yl)-2-chlorobenzaldehyde thiosemicarbazone	389
306		4-[4-(3-chlorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	425
307		4-[4-(3-chlorobenzyl)piperazin-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	407
308		4-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]-2,3-difluorobenzaldehyde thiosemicarbazone	434

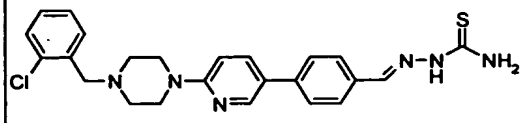
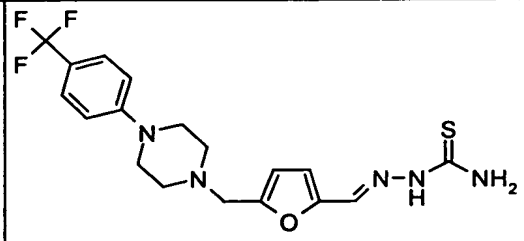
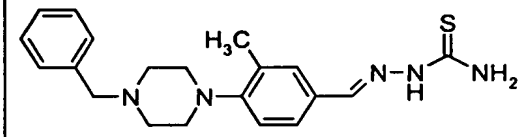
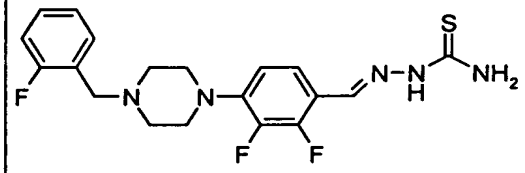
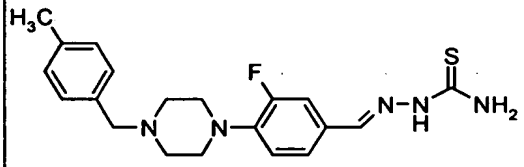
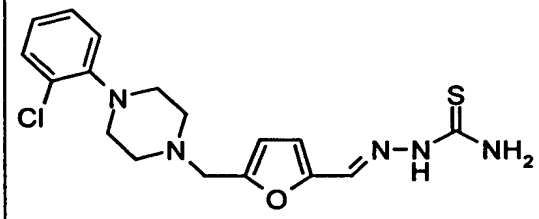
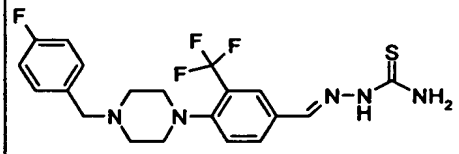
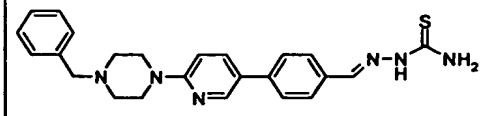
TABLE 3			
	Structur	Name	MH+
309		4-{6-[4-(2-chlorobenzyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	466
310		5-({4-[4-(trifluoromethyl)phenyl]piperazin-1-yl}methyl)-2-furaldehyde thiosemicarbazone	412
311		4-(4-benzylpiperazin-1-yl)-3-methylbenzaldehyde thiosemicarbazone	369
312		2,3-difluoro-4-[4-(2-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	408
313		3-fluoro-4-[4-(4-methylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	387
314		5-{[4-(2-chlorophenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	379
315		4-[4-(4-fluorobenzyl)piperazin-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	440
316		4-[6-(4-benzylpiperazin-1-yl)pyridin-3-yl]benzaldehyde thiosemicarbazone	432

TABLE 3

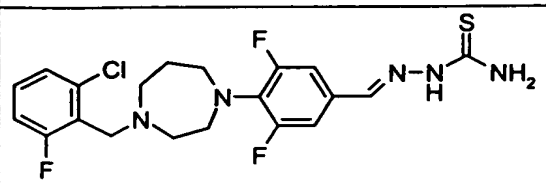
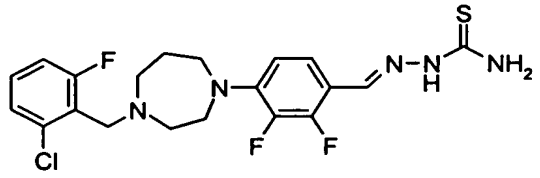
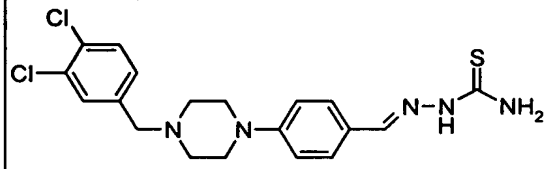
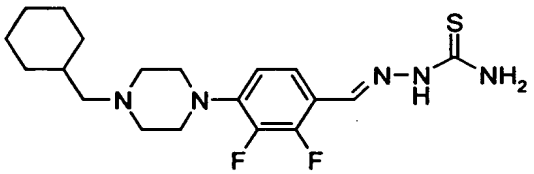
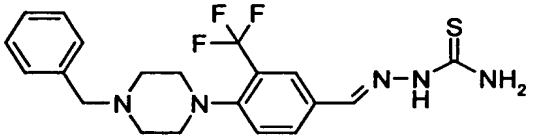
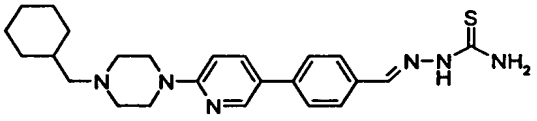
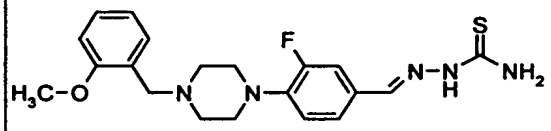
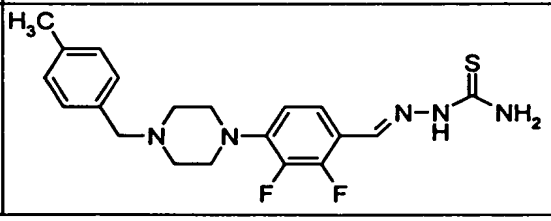
	Structure	Name	MH+
317		4-[4-(2-chloro-6-fluorobenzyl)-1,4-diazepan-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	457
318		4-[4-(2-chloro-6-fluorobenzyl)-1,4-diazepan-1-yl]-2,3-difluorobenzaldehyde thiosemicarbazone	457
319		4-[4-(3,4-dichlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	423
320		4-[4-(cyclohexylmethyl)piperazin-1-yl]-2,3-difluorobenzaldehyde thiosemicarbazone	397
321		4-(4-benzylpiperazin-1-yl)-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	422
322		4-{6-[4-(cyclohexylmethyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	438
323		3-fluoro-4-[4-(2-methoxybenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	403
324		2,3-difluoro-4-[4-(4-methylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404

TABLE 3

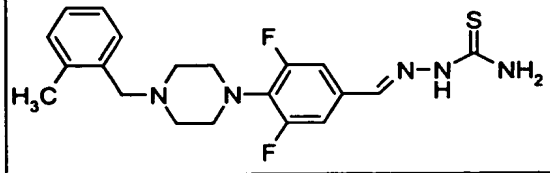
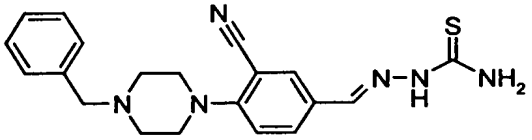
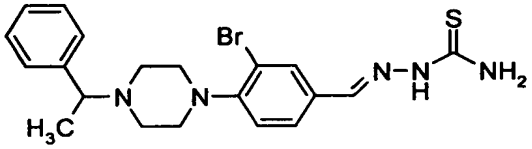
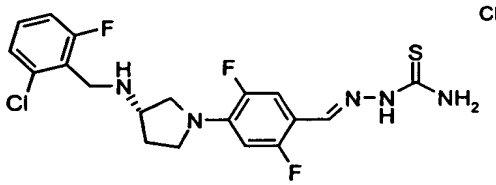
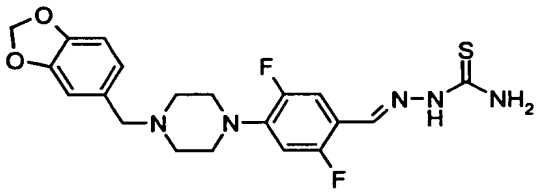
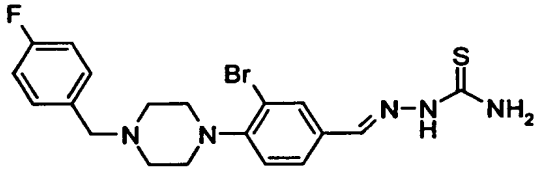
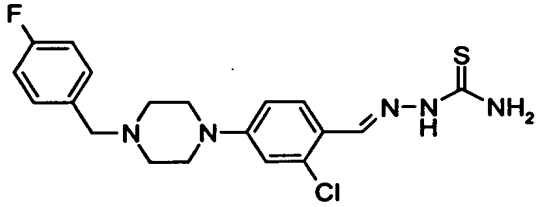
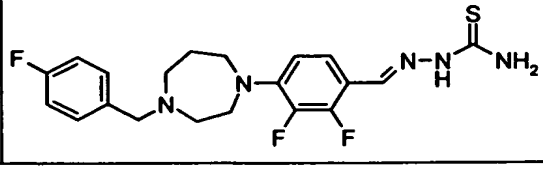
	Structur	Nam	MH+
325		3,5-difluoro-4-[4-(2-methylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404
326		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-(4-benzylpiperazin-1-yl)benzonitrile	380
327		3-bromo-4-[4-(1-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	447
328		4-{(3S)-3-[(2-chloro-6-fluorobenzyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	443
329		4-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	434
330		3-bromo-4-[4-(4-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	451
331		2-chloro-4-[4-(4-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	407
332		2,3-difluoro-4-[4-(4-fluorobenzyl)-1,4-diazepan-1-yl]benzaldehyde thiosemicarbazone	422

TABLE 3

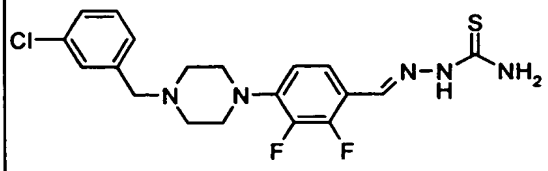
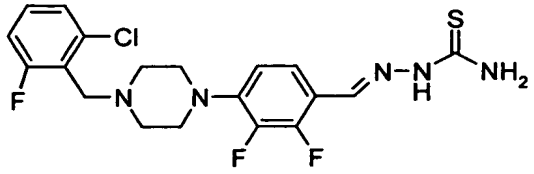
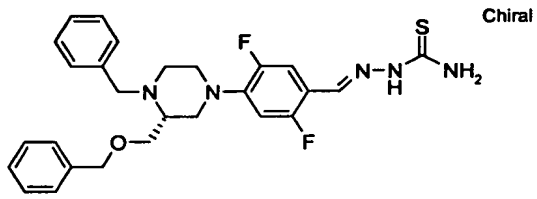
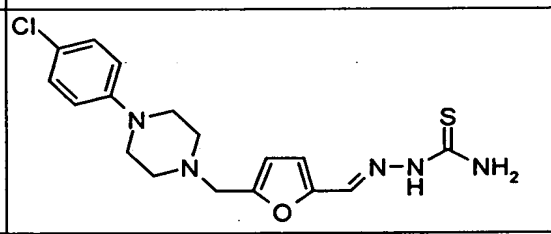
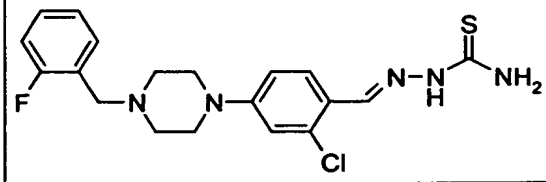
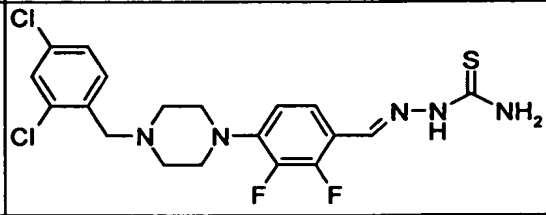
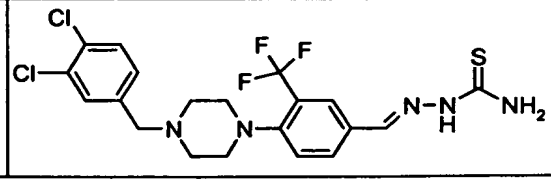
	Structure	Name	MH+
333		4-[4-(3-chlorobenzyl)piperazin-1-yl]-2,3-difluorobenzaldehyde thiosemicarbazone	425
334		4-[4-(2-chloro-6-fluorobenzyl)piperazin-1-yl]-2,3-difluorobenzaldehyde thiosemicarbazone	443
335		4-{(3R)-4-benzyl-3-[(benzyloxy)methyl]piperazin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	511
336		5-{[4-(4-chlorophenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	379
337		2-chloro-4-[4-(2-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	407
338		4-[4-(2,4-dichlorobenzyl)piperazin-1-yl]-2,3-difluorobenzaldehyde thiosemicarbazone	459
339		4-[4-(3,4-dichlorobenzyl)piperazin-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	491

TABLE 3

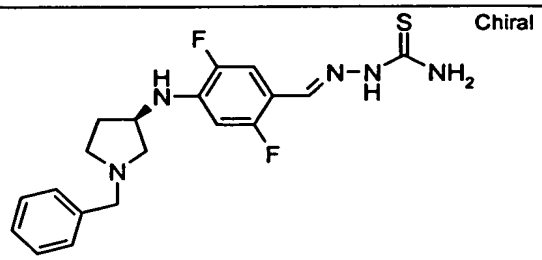
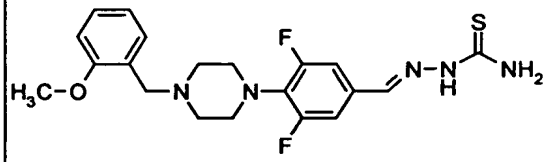
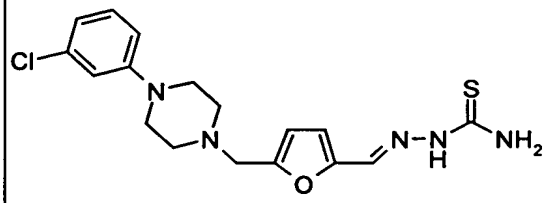
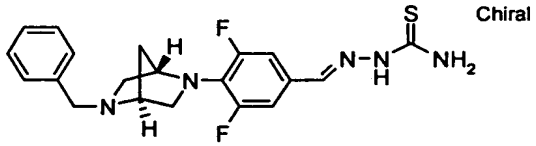
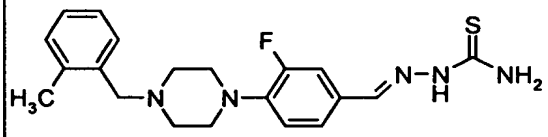
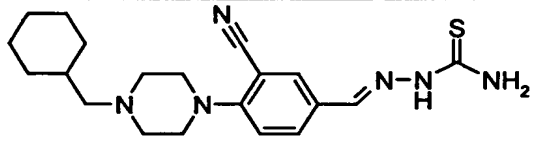
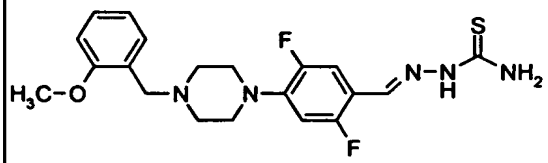
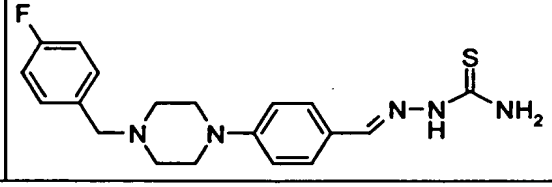
	Structure	Name	MH+
340	 Chiral	4-{[(3R)-1-benzylpyrrolidin-3-yl]amino}-2,5-difluorobenzaldehyde thiosemicarbazone	390
341		3,5-difluoro-4-[4-(2-methoxybenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	420
342		5-{[4-(3-chlorophenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	379
343	 Chiral	4-[(1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	402
344		3-fluoro-4-[4-(2-methylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	387
345		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-[4-(cyclohexylmethyl)piperazin-1-yl]benzonitrile	386
346		2,5-difluoro-4-[4-(2-methoxybenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	420
347		4-[4-(4-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	372

TABLE 3

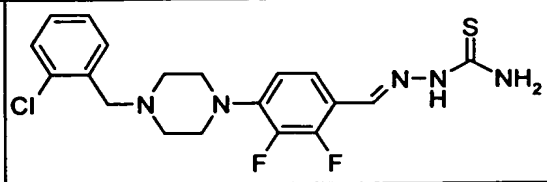
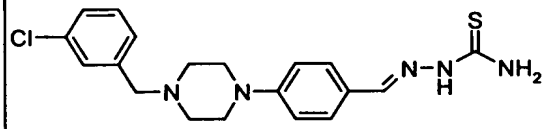
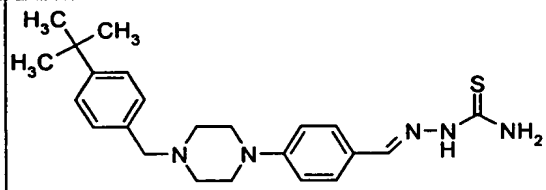
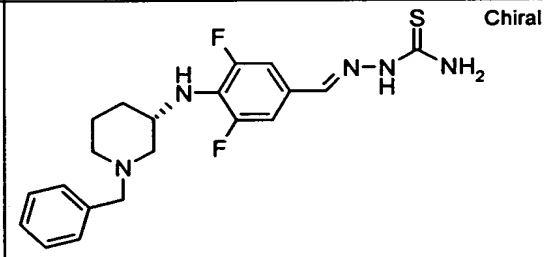
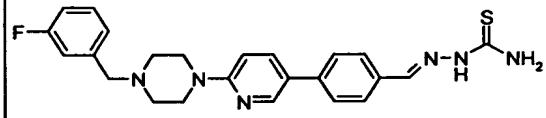
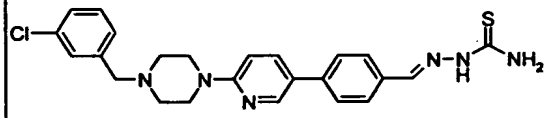
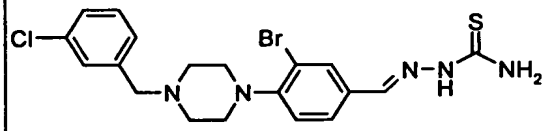
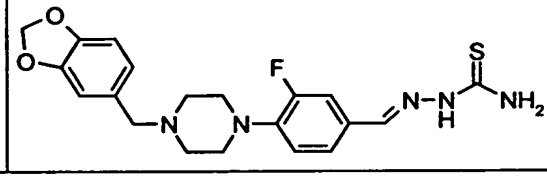
	Structure	Name	MH+
348		4-[4-(2-chlorobenzyl)piperazin-1-yl]-2,3-difluorobenzaldehyde thiosemicarbazone	425
349		4-[4-(3-chlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	389
350		4-[4-(4-tert-butylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	411
351		4-{[(3S)-1-benzylpiperidin-3-yl]amino}-3,5-difluorobenzaldehyde thiosemicarbazone	404
352		4-{6-[4-(3-fluorobenzyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	450
353		4-{6-[4-(3-chlorobenzyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	466
354		3-bromo-4-[4-(3-chlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	468
355		4-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	416

TABLE 3

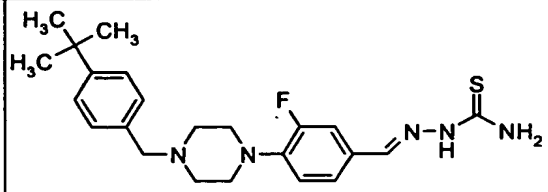
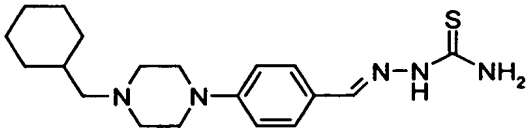
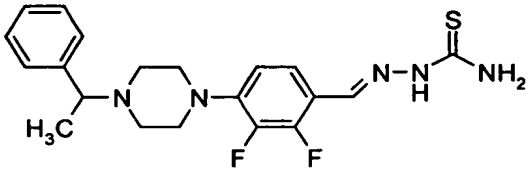
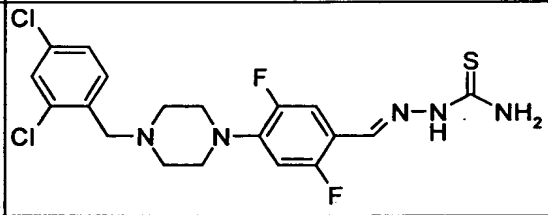
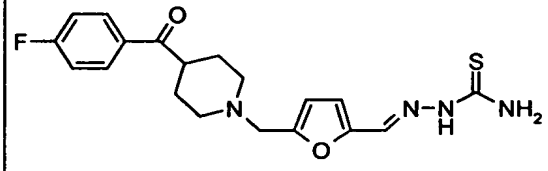
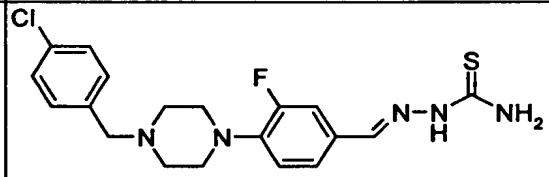
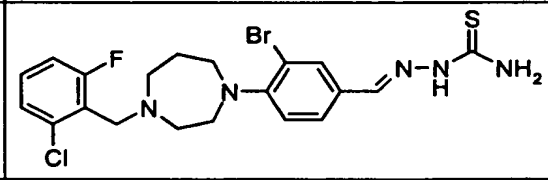
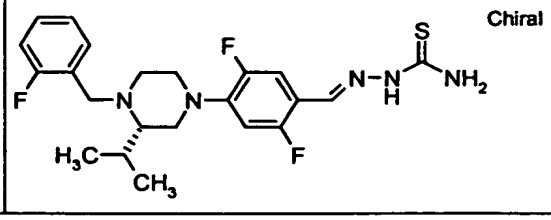
	Structure	Name	MH+
356		4-[4-(4-tert-butylbenzyl)piperazin-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	429
357		4-[4-(cyclohexylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	361
358		2,3-difluoro-4-[4-(1-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404
359		4-[4-(2,4-dichlorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	459
360		5-{[4-(4-fluorobenzoyl)piperidin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	389
361		4-[4-(4-chlorobenzyl)piperazin-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	407
362		3-bromo-4-[4-(2-chloro-6-fluorobenzyl)-1,4-diazepan-1-yl]benzaldehyde thiosemicarbazone	500
363		2,5-difluoro-4-[(3S)-4-(2-fluorobenzyl)-3-isopropylpiperazin-1-yl]benzaldehyde thiosemicarbazone	451

TABLE 3

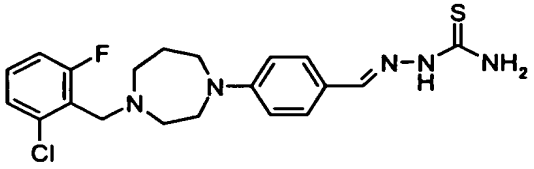
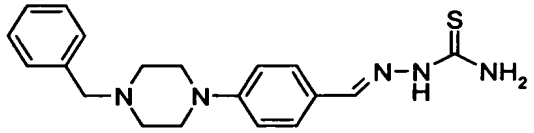
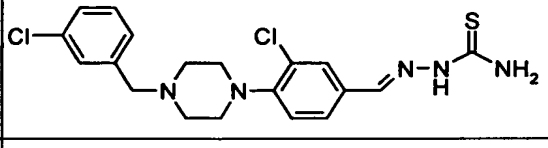
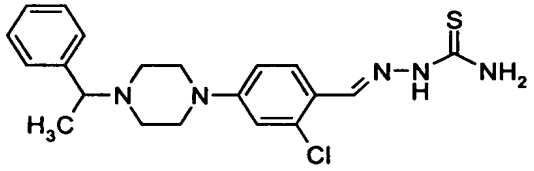
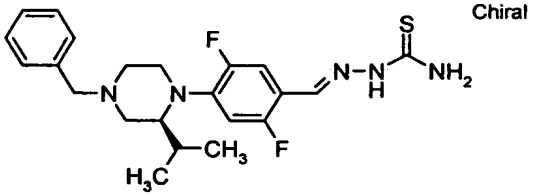
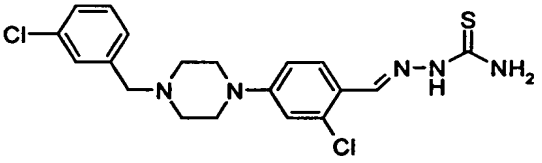
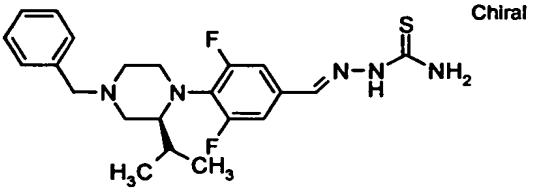
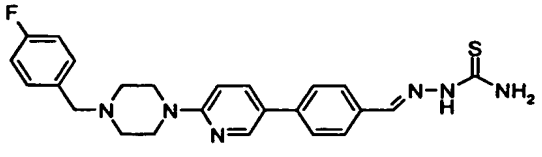
	Structure	Name	MH+
364		4-[4-(2-chloro-6-fluorobenzyl)-1,4-diazepan-1-yl]benzaldehyde thiosemicarbazone	421
365		4-(4-benzylpiperazin-1-yl)benzaldehyde thiosemicarbazone	354
366		3-chloro-4-[4-(3-chlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	423
367		2-chloro-4-[4-(1-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	403
368	 Chiral	4-[(2S)-4-benzyl-2-isopropylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	433
369		2-chloro-4-[4-(3-chlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	423
370	 Chiral	4-[(2S)-4-benzyl-2-isopropylpiperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	433
371		4-{6-[4-(4-fluorobenzyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	450

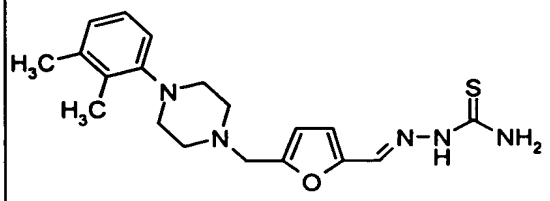
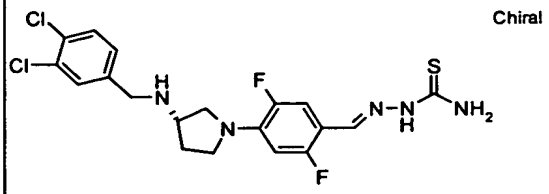
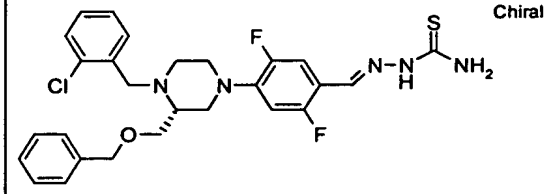
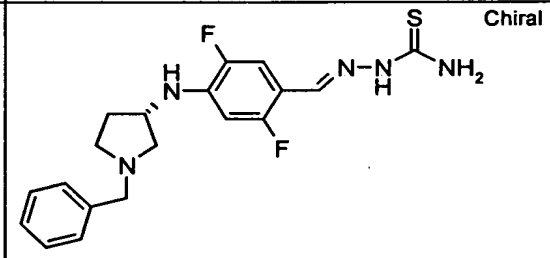
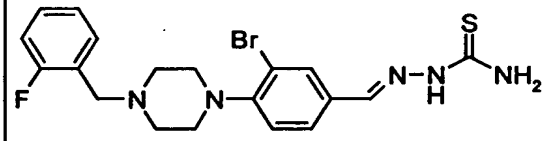
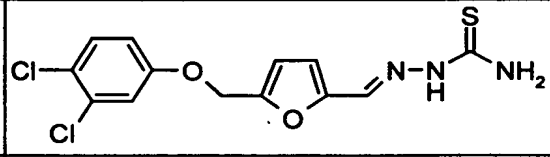
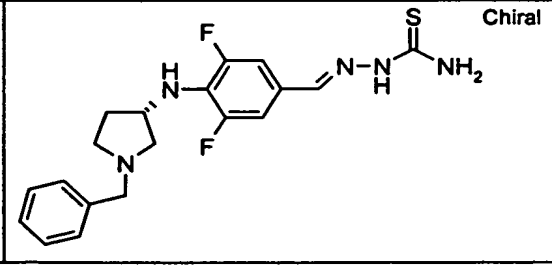
TABLE 3			
	Structur	Name	MH+
372		5-{[4-(2,3-dimethylphenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	373
373	 Chiral	4-{(3S)-3-[(3,4-dichlorobenzyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	459
374	 Chiral	4-[(3R)-3-[(benzyloxy)methyl]-4-(2-chlorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	545
375	 Chiral	4-{[(3S)-1-benzylpyrrolidin-3-yl]amino}-2,5-difluorobenzaldehyde thiosemicarbazone	390
376		3-bromo-4-[4-(2-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	451
377		5-[(3,4-dichlorophenoxy)methyl]-2-furaldehyde thiosemicarbazone	345
378	 Chiral	4-{[(3S)-1-benzylpyrrolidin-3-yl]amino}-3,5-difluorobenzaldehyde thiosemicarbazone	390

TABLE 3

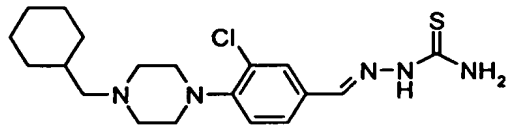
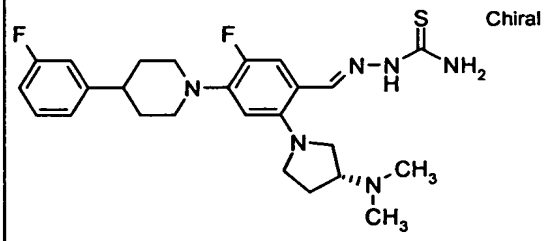
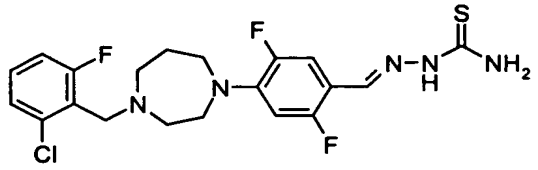
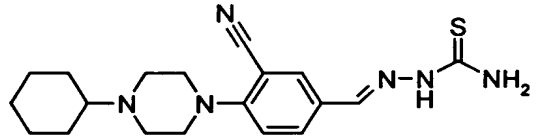
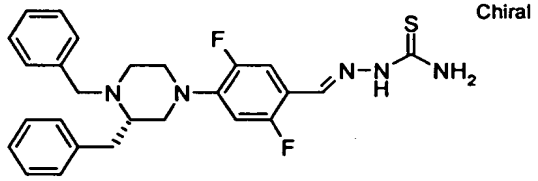
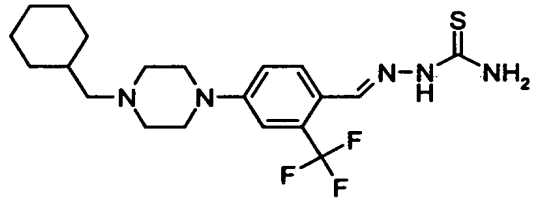
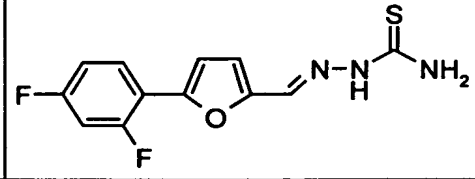
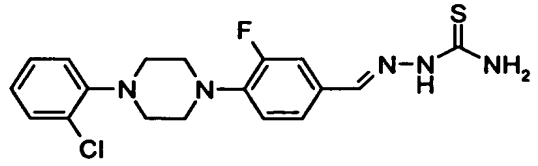
	Structure	Name	MH+
379		3-chloro-4-[4-(cyclohexylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	395
380		2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-[4-(3-fluorophenyl)piperidin-1-yl]benzaldehyde thiosemicarbazone	488
381		4-[4-(2-chloro-6-fluorobenzyl)-1,4-diazepan-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	457
382		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-(4-cyclohexylpiperazin-1-yl)benzonitrile	372
383		4-[(3S)-3,4-dibenzylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	481
384		4-[4-(cyclohexylmethyl)piperazin-1-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	429
385		5-(2,4-difluorophenyl)-2-furaldehyde thiosemicarbazone	282
386		4-[4-(2-chlorophenyl)piperazin-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	393

TABLE 3

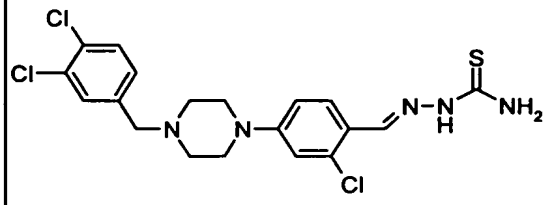
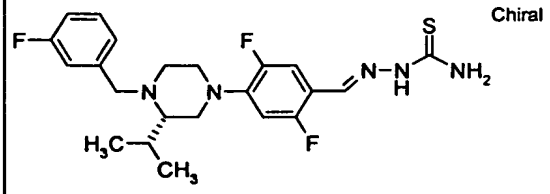
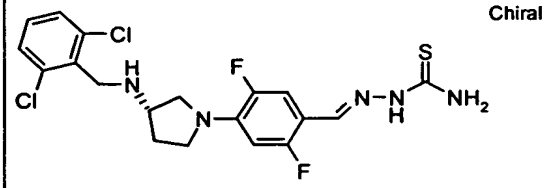
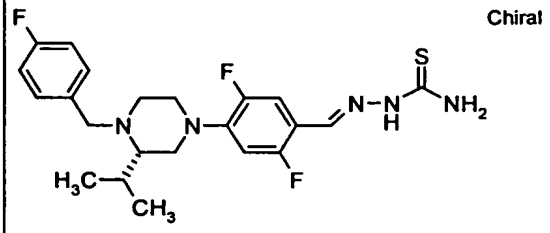
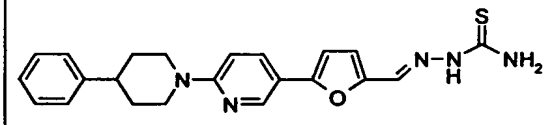
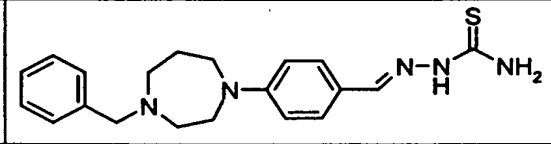
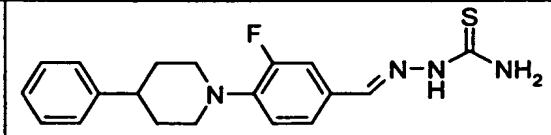
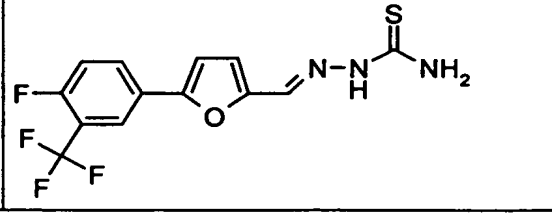
	Structure	Name	MH+
387		2-chloro-4-[4-(3,4-dichlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	458
388	 Chiral	2,5-difluoro-4-[(3S)-4-(3-fluorobenzyl)-3-isopropylpiperazin-1-yl]benzaldehyde thiosemicarbazone	451
389	 Chiral	4-{(3S)-3-[(2,6-dichlorobenzyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	459
390	 Chiral	2,5-difluoro-4-[(3S)-4-(4-fluorobenzyl)-3-isopropylpiperazin-1-yl]benzaldehyde thiosemicarbazone	451
391		5-[6-(4-phenylpiperidin-1-yl)pyridin-3-yl]-2-furaldehyde thiosemicarbazone	407
392		4-(4-benzyl-1,4-diazepan-1-yl)benzaldehyde thiosemicarbazone	369
393		3-fluoro-4-(4-phenylpiperidin-1-yl)benzaldehyde thiosemicarbazone	357
394		5-[4-fluoro-3-(trifluoromethyl)phenyl]-2-furaldehyde thiosemicarbazone	332

TABLE 3

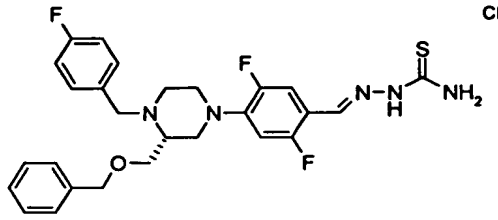
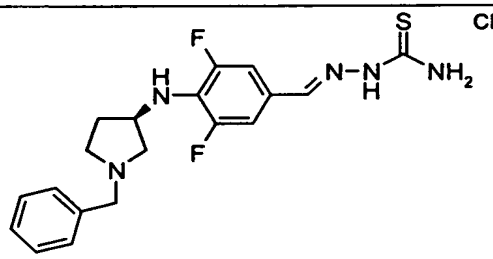
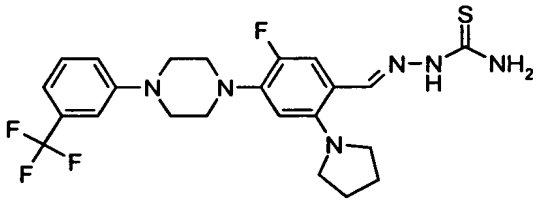
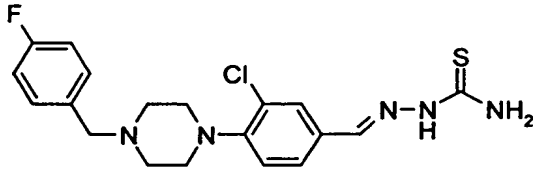
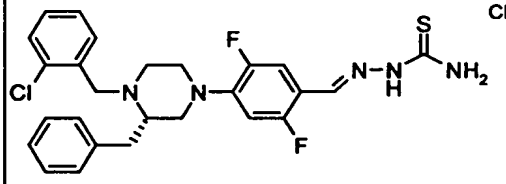
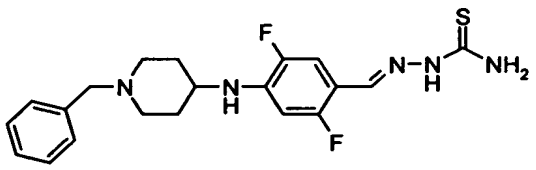
	Structure	Name	MH+
395	 Chiral	4-[(3R)-3-[(benzyloxy)methyl]-4-(4-fluorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	529
396	 Chiral	4-{[(3R)-1-benzylpyrrolidin-3-yl]amino}-3,5-difluorobenzaldehyde thiosemicarbazone	390
397		5-fluoro-2-pyrrolidin-1-yl-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	496
398		3-chloro-4-[4-(4-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	407
399	 Chiral	4-[(3S)-3-benzyl-4-(2-chlorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	515
400		4-[(1-benzylpiperidin-4-yl)amino]-2,5-difluorobenzaldehyde thiosemicarbazone	404

TABLE 3

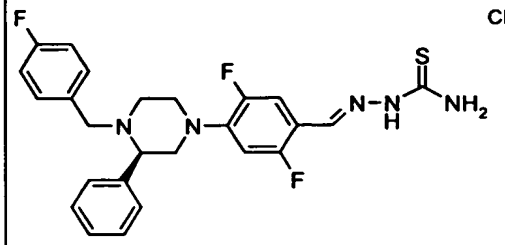
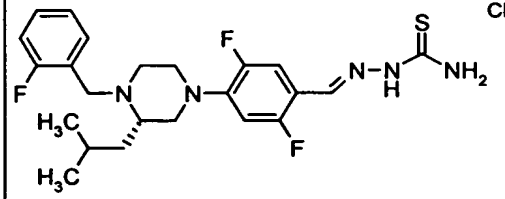
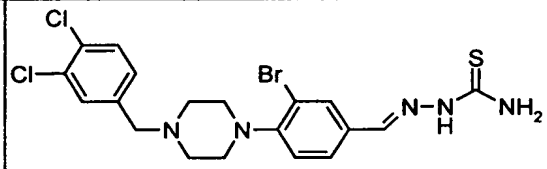
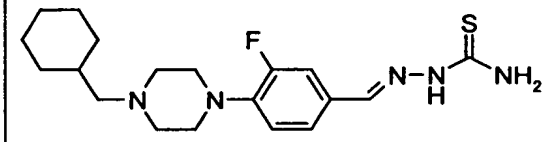
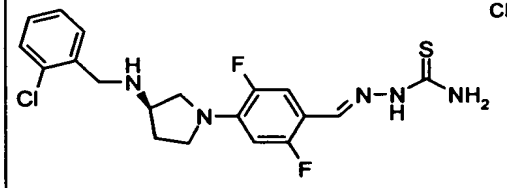
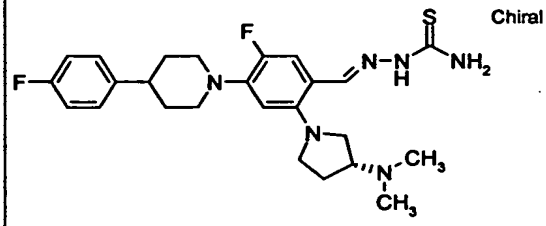
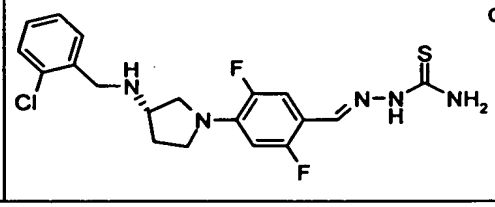
	Structure	Name	MH+
401	 Chiral	2,5-difluoro-4-[(3R)-4-(4-fluorobenzyl)-3-phenylpiperazin-1-yl]benzaldehyde thiosemicarbazone	485
402	 Chiral	2,5-difluoro-4-[(3S)-4-(2-fluorobenzyl)-3-isobutylpiperazin-1-yl]benzaldehyde thiosemicarbazone	465
403		3-bromo-4-[4-(3,4-dichlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	502
404		4-[4-(cyclohexylmethyl)piperazin-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	379
405	 Chiral	4-{(3R)-3-[(2-chlorobenzyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	425
406	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-[4-(4-fluorophenyl)piperidin-1-yl]benzaldehyde thiosemicarbazone	488
407	 Chiral	4-{(3S)-3-[(2-chlorobenzyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	425

TABLE 3

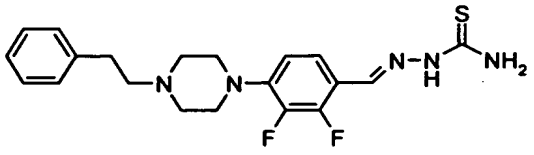
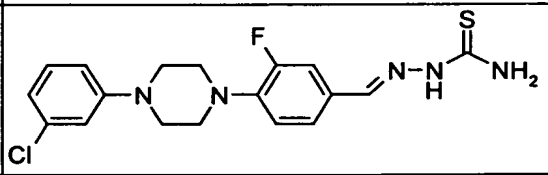
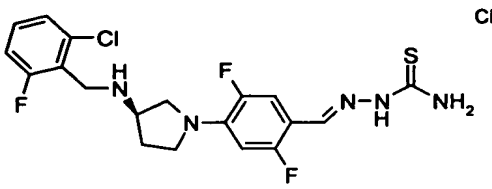
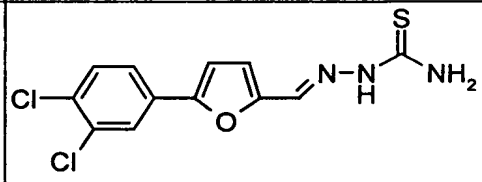
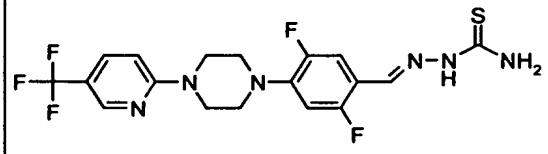
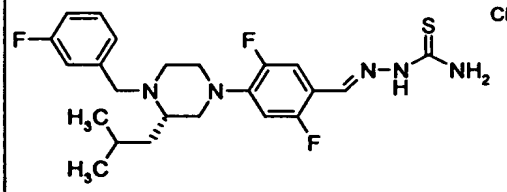
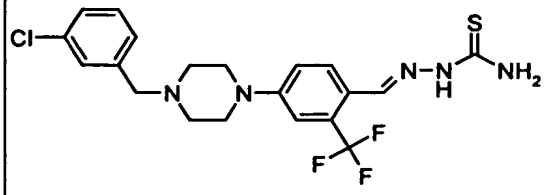
	Structur	Name	MH+
408		2,3-difluoro-4-[4-(2-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404
409		4-[4-(3-chlorophenyl)piperazin-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	393
410	 Chiral	4-{(3R)-3-[(2-chloro-6-fluorobenzyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	443
411		5-(3,4-dichlorophenyl)-2-furaldehyde thiosemicarbazone	315
412		2,5-difluoro-4-{4-[5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}benzaldehyde thiosemicarbazone	445
413	 Chiral	2,5-difluoro-4-[(3S)-4-(3-fluorobenzyl)-3-isobutylpiperazin-1-yl]benzaldehyde thiosemicarbazone	465
414		4-(4-cyclohexylpiperazin-1-yl)-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	415
415		4-[4-(3-chlorobenzyl)piperazin-1-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	457

TABLE 3

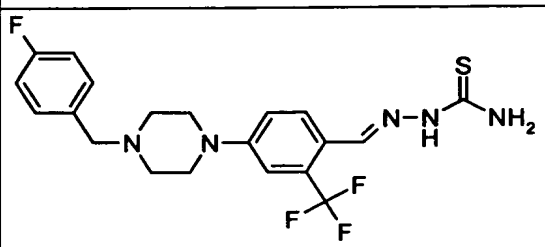
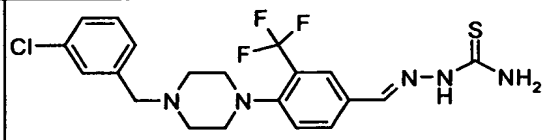
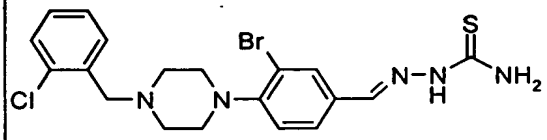
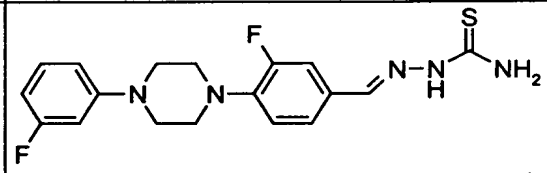
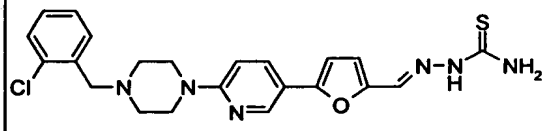
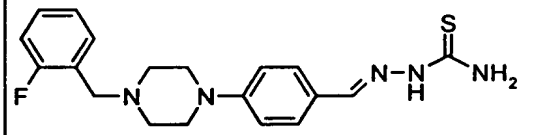
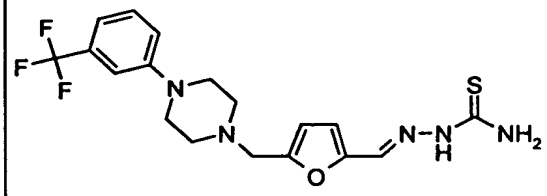
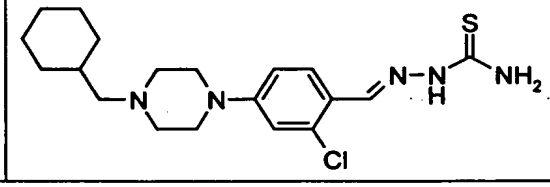
	Structure	Name	MH+
416		4-[4-(4-fluorobenzyl)piperazin-1-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	440
417		4-[4-(3-chlorobenzyl)piperazin-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	457
418		3-bromo-4-[4-(2-chlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	468
419		3-fluoro-4-[4-(3-fluorophenyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	376
420		5-{6-[4-(2-chlorobenzyl)piperazin-1-yl]pyridin-3-yl}-2-furaldehyde thiosemicarbazone	456
421		4-[4-(2-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	372
422		5-({4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}methyl)-2-furaldehyde thiosemicarbazone	412
423		2-chloro-4-[4-(cyclohexylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	395

TABLE 3

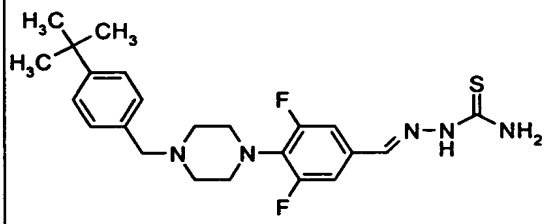
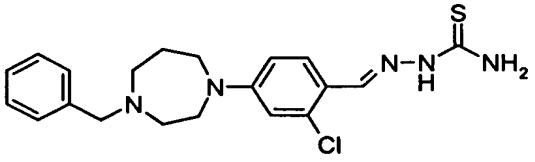
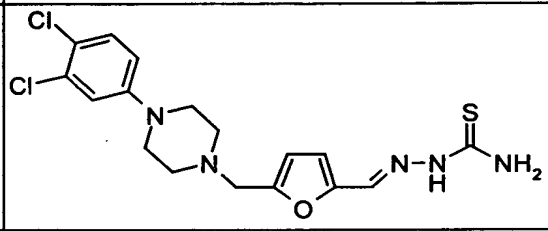
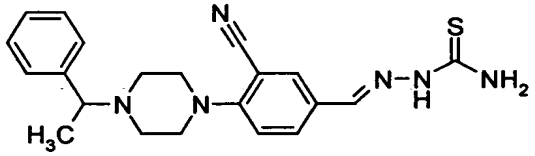
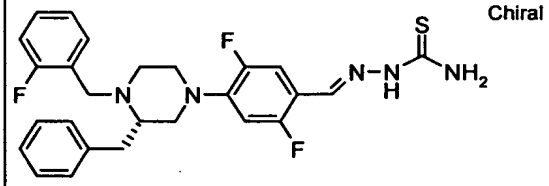
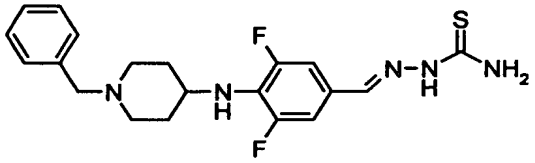
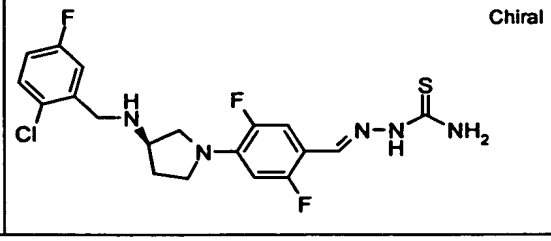
	Structure	Name	MH+
424		4-[4-(4-tert-butylbenzyl)piperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	447
425		4-(4-benzyl-1,4-diazepan-1-yl)-2-chlorobenzaldehyde thiosemicarbazone	403
426		5-{[4-(3,4-dichlorophenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	413
427		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-[4-(1-phenylethyl)piperazin-1-yl]benzonitrile	394
428	 Chiral	4-[(3S)-3-benzyl-4-(2-fluorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	499
429		4-[(1-benzylpiperidin-4-yl)amino]-3,5-difluorobenzaldehyde thiosemicarbazone	404
430	 Chiral	4-{(3R)-3-[(2-chloro-5-fluorobenzyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	443

TABLE 3

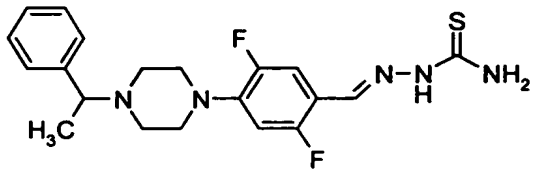
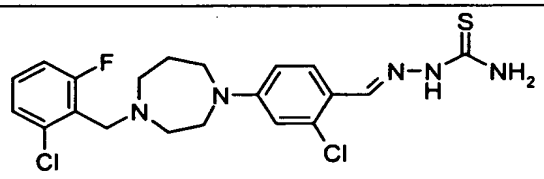
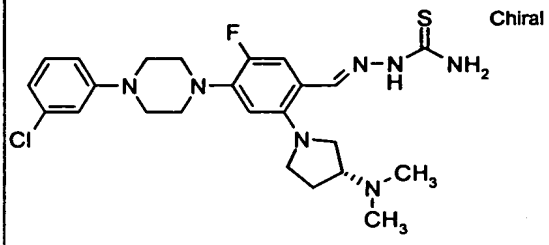
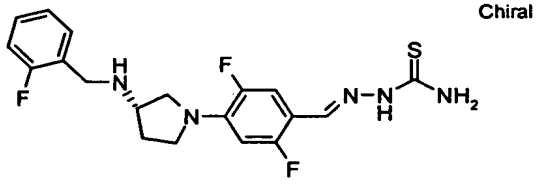
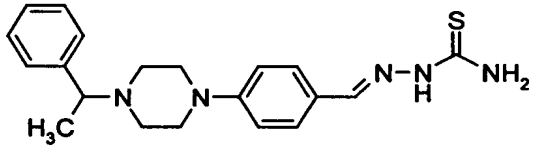
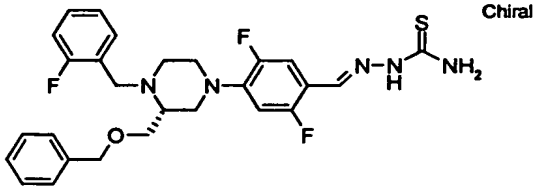
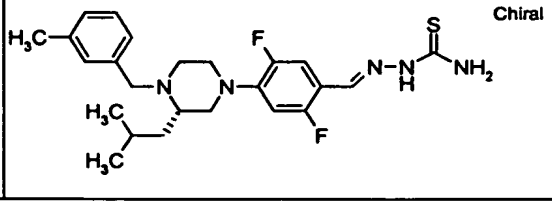
	Structur	Name	MH+
431		2,5-difluoro-4-[4-(1-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404
432		2-chloro-4-[4-(2-chloro-6-fluorobenzyl)-1,4-diazepan-1-yl]benzaldehyde thiosemicarbazone	455
433	 Chiral	4-[4-(3-chlorophenyl)piperazin-1-yl]-2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	505
434	 Chiral	2,5-difluoro-4-{(3S)-3-[(2-fluorobenzyl)amino]pyrrolidin-1-yl}benzaldehyde thiosemicarbazone	408
435		4-[4-(1-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	369
436	 Chiral	4-[(3R)-3-[(benzyloxy)methyl]-4-(2-fluorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	529
437	 Chiral	2,5-difluoro-4-[(3S)-3-isobutyl-4-(3-methylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	461

TABLE 3

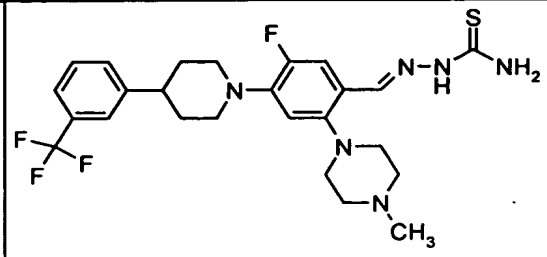
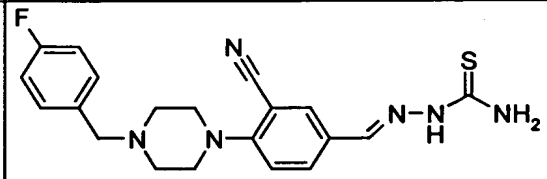
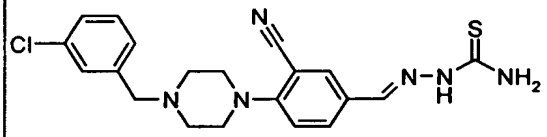
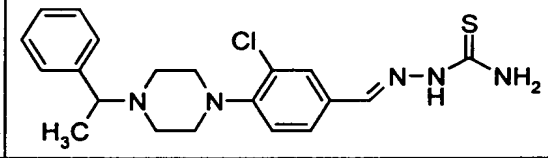
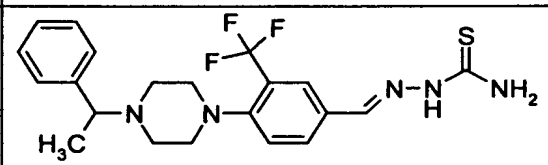
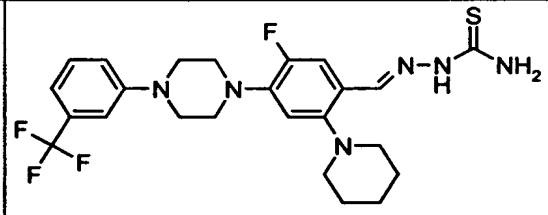
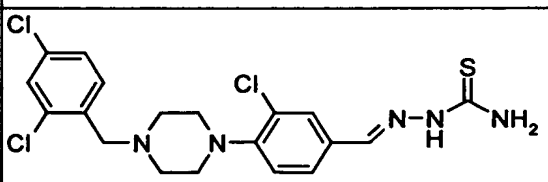
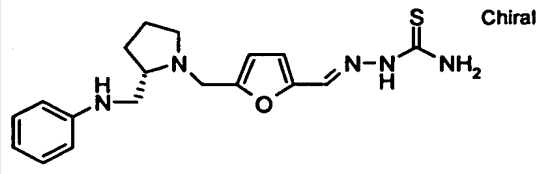
	Structure	Name	MH+
438		5-fluoro-2-(4-methylpiperazin-1-yl)-4-{4-[3-(trifluoromethyl)phenyl]piperidin-1-yl}benzaldehyde thiosemicarbazone	524
439		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-[4-(4-fluorobenzyl)piperazin-1-yl]benzonitrile	397
440		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-[4-(3-chlorobenzyl)piperazin-1-yl]benzonitrile	414
441		3-chloro-4-[4-(1-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	403
442		4-[4-(1-phenylethyl)piperazin-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	437
443		5-fluoro-2-piperidin-1-yl-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	510
444		3-chloro-4-[4-(2,4-dichlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	458
445	 Chiral	5-{[(2S)-2-(anilinomethyl)pyrrolidin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	358

TABLE 3

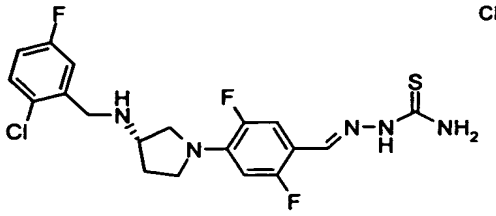
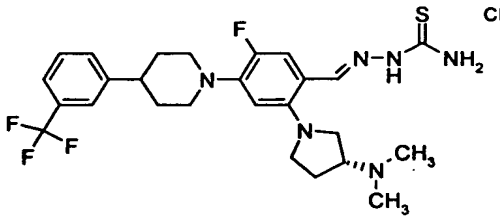
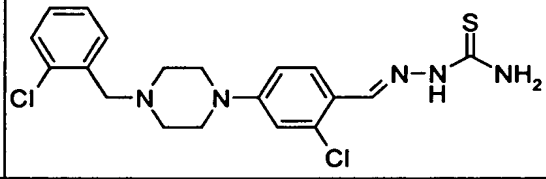
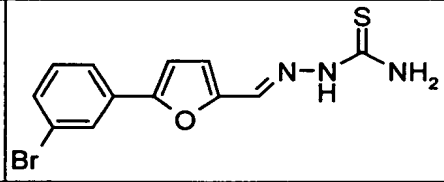
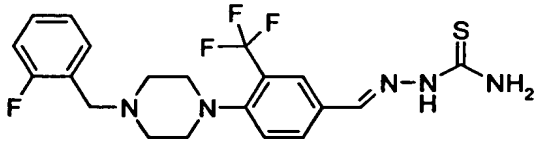
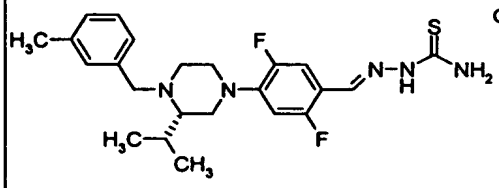
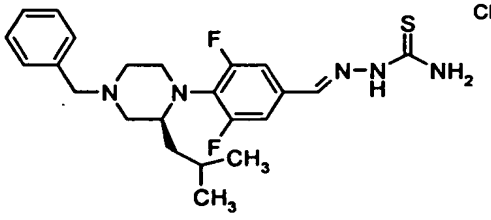
	Structure	Name	MH+
446	 Chiral	4-{(3S)-3-[(2-chloro-5-fluorobenzyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	443
447	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-{4-[3-(trifluoromethyl)phenyl]piperidin-1-yl}benzaldehyde thiosemicarbazone	538
448		2-chloro-4-[4-(2-chlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	423
449		5-(3-bromophenyl)-2-furaldehyde thiosemicarbazone	325
450		4-[4-(2-fluorobenzyl)piperazin-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	440
451	 Chiral	2,5-difluoro-4-[(3S)-3-isopropyl-4-(3-methylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	447
452	 Chiral	4-[(2S)-4-benzyl-2-isobutylpiperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	447

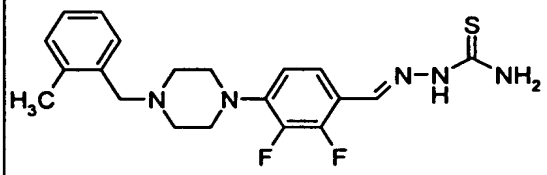
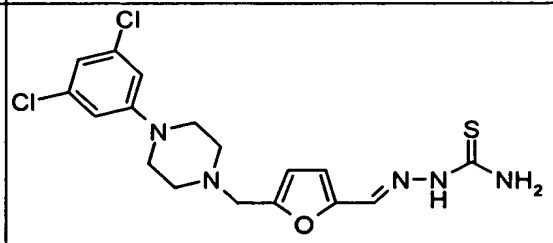
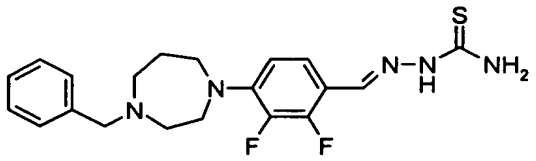
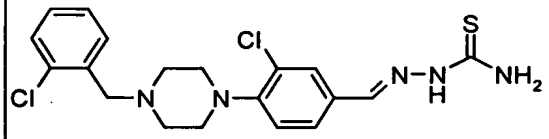
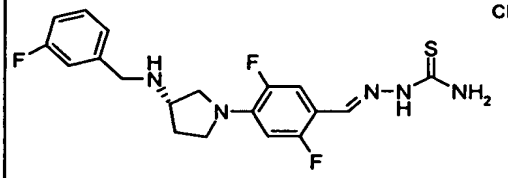
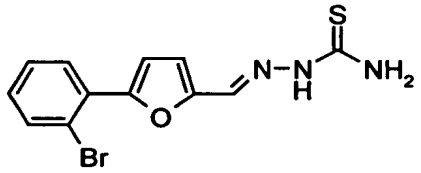
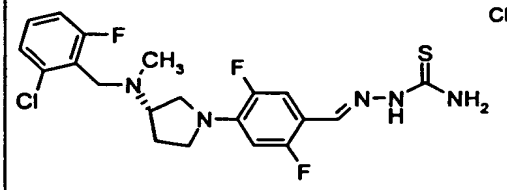
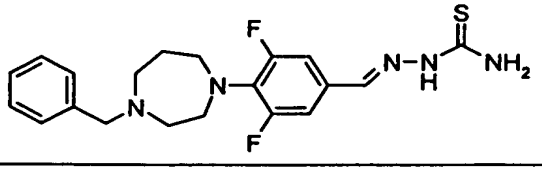
TABLE 3			
	Structure	Name	MH+
453		2,3-difluoro-4-[4-(2-methylbenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404
454		5-{[4-(3,5-dichlorophenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	413
455		4-(4-benzyl-1,4-diazepan-1-yl)-2,3-difluorobenzaldehyde thiosemicarbazone	404
456		3-chloro-4-[4-(2-chlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	423
457	Chiral 	2,5-difluoro-4-{(3S)-3-[(3-fluorobenzyl)amino]pyrrolidin-1-yl}benzaldehyde thiosemicarbazone	408
458		5-(2-bromophenyl)-2-furaldehyde thiosemicarbazone	325
459	Chiral 	4-{(3S)-3-[(2-chloro-6-fluorobenzyl)(methyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	457
460		4-(4-benzyl-1,4-diazepan-1-yl)-3,5-difluorobenzaldehyde thiosemicarbazone	404

TABLE 3

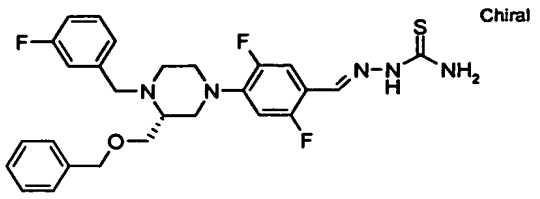
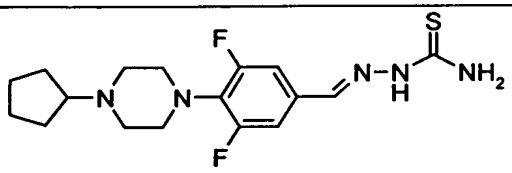
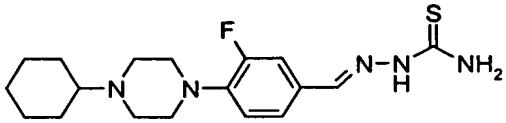
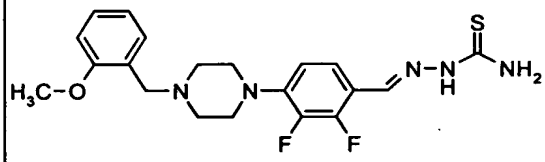
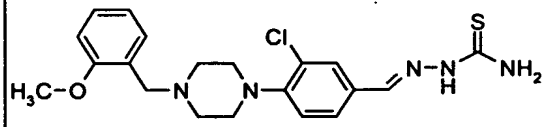
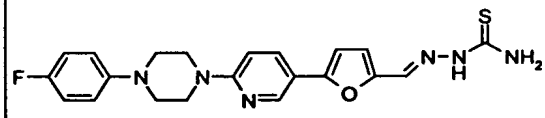
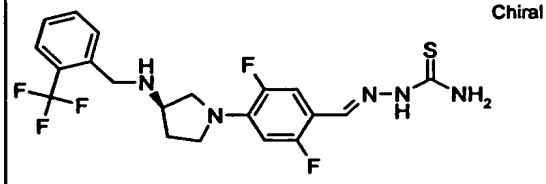
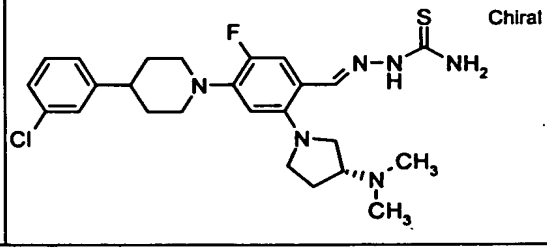
	Structure	Name	MH+
461	 Chiral	4-[(3R)-3-[(benzyloxy)methyl]-4-(3-fluorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	529
462		4-(4-cyclopentylpiperazin-1-yl)-3,5-difluorobenzaldehyde thiosemicarbazone	368
463		4-(4-cyclohexylpiperazin-1-yl)-3-fluorobenzaldehyde thiosemicarbazone	365
464		2,3-difluoro-4-[4-(2-methoxybenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	420
465		3-chloro-4-[4-(2-methoxybenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	419
466		5-{6-[4-(4-fluorophenyl)piperazin-1-yl]pyridin-3-yl}-2-furaldehyde thiosemicarbazone	426
467	 Chiral	2,5-difluoro-4-((3R)-3-{[2-(trifluoromethyl)benzyl]amino}pyrrolidin-1-yl)benzaldehyde thiosemicarbazone	458
468	 Chiral	4-[4-(3-chlorophenyl)piperidin-1-yl]-2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	504

TABLE 3

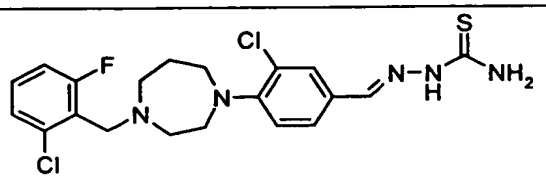
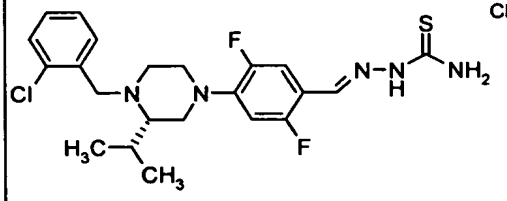
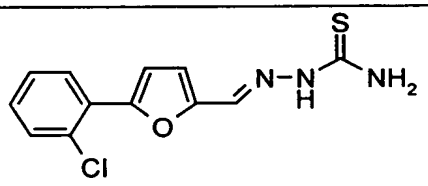
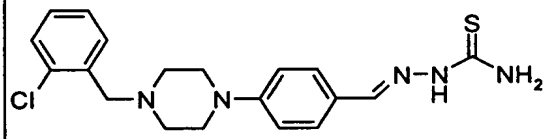
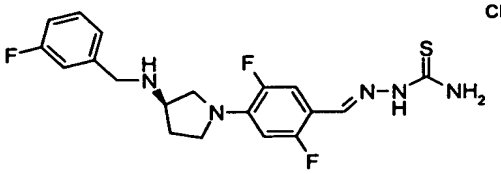
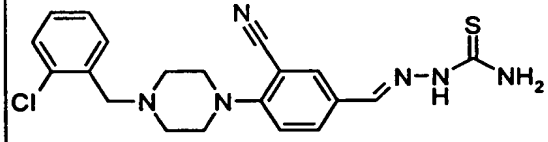
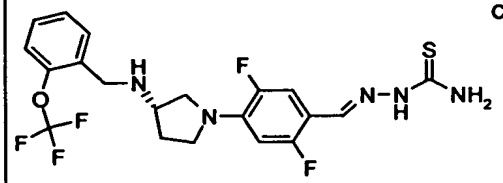
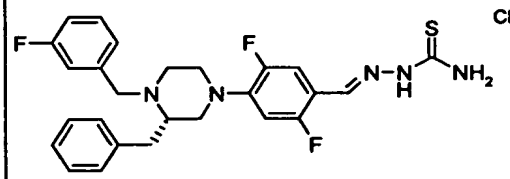
	Structur	Name	MH+
469		3-chloro-4-[4-(2-chloro-6-fluorobenzyl)-1,4-diazepan-1-yl]benzaldehyde thiosemicarbazone	455
470	 Chiral	4-[(3S)-4-(2-chlorobenzyl)-3-isopropylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	467
471		5-(2-chlorophenyl)-2-furaldehyde thiosemicarbazone	281
472		4-[4-(2-chlorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	389
473	 Chiral	2,5-difluoro-4-{(3R)-3-[(3-fluorobenzyl)amino]pyrrolidin-1-yl}benzaldehyde thiosemicarbazone	408
474		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-[4-(2-chlorobenzyl)piperazin-1-yl]benzonitrile	414
475	 Chiral	2,5-difluoro-4-((3S)-3-{[2-(trifluoromethoxy)benzyl]amino}pyrrolidin-1-yl)benzaldehyde thiosemicarbazone	474
476	 Chiral	4-[(3S)-3-benzyl-4-(3-fluorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	499

TABLE 3

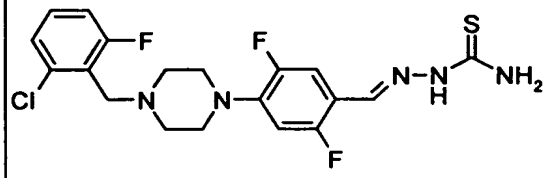
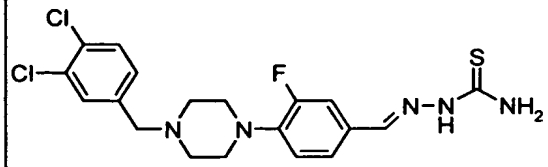
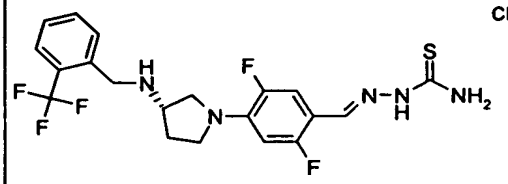
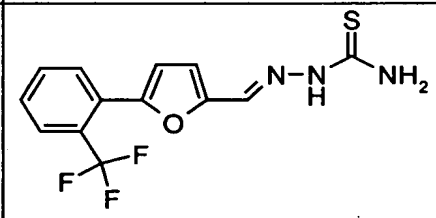
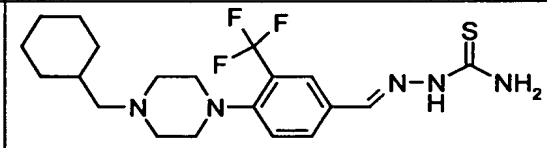
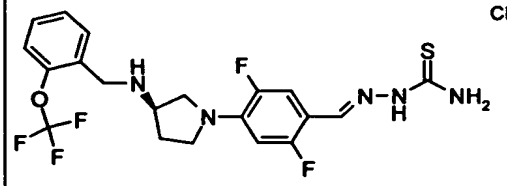
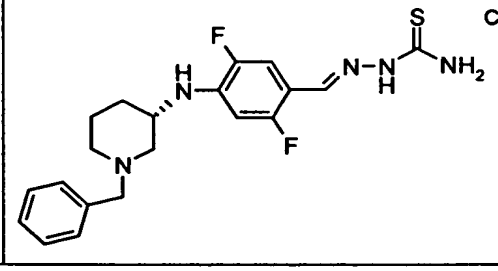
	Structure	Name	MH+
477		4-[4-(2-chloro-6-fluorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	443
478		4-[4-(3,4-dichlorobenzyl)piperazin-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	441
479	 Chiral	2,5-difluoro-4-((3S)-3-{[2-(trifluoromethyl)benzyl]amino}pyrrolidin-1-yl)benzaldehyde thiosemicarbazone	458
480		5-[2-(trifluoromethyl)phenyl]-2-furaldehyde thiosemicarbazone	314
481		4-[4-(cyclohexylmethyl)piperazin-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	429
482	 Chiral	2,5-difluoro-4-((3R)-3-{[2-(trifluoromethoxy)benzyl]amino}pyrrolidin-1-yl)benzaldehyde thiosemicarbazone	474
483	 Chiral	4-{[(3S)-1-benzylpiperidin-3-yl]amino}-2,5-difluorobenzaldehyde thiosemicarbazone	404

TABLE 3

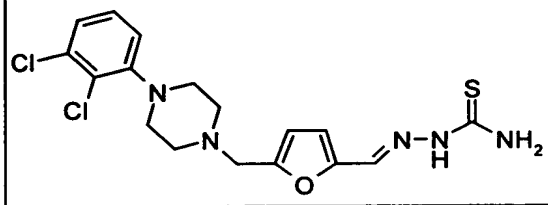
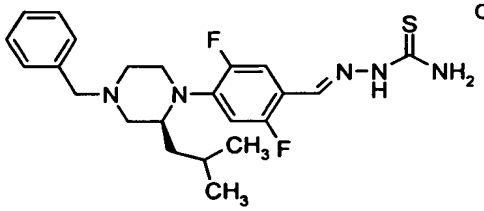
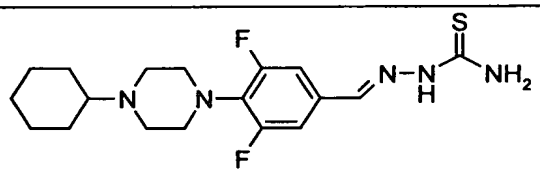
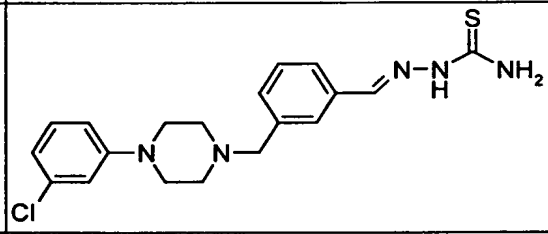
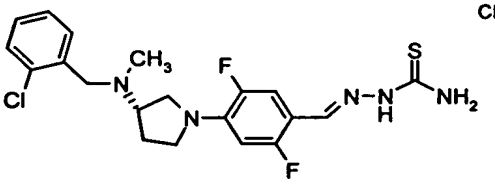
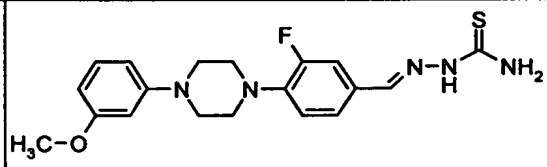
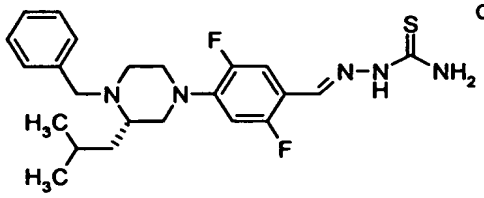
	Structur	Name	MH+
484		5-{[4-(2,3-dichlorophenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	413
485	 Chiral	4-[(2S)-4-benzyl-2-isobutylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	447
486		4-(4-cyclohexylpiperazin-1-yl)-3,5-difluorobenzaldehyde thiosemicarbazone	382
487		3-{[4-(3-chlorophenyl)piperazin-1-yl]methyl}benzaldehyde thiosemicarbazone	389
488	 Chiral	4-{(3S)-3-[(2-chlorobenzyl)(methyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	439
489		3-fluoro-4-[4-(3-methoxyphenyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	388
490	 Chiral	4-[(3S)-4-benzyl-3-isobutylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	447

TABLE 3

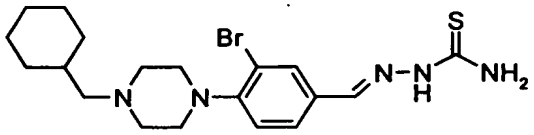
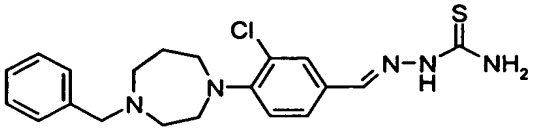
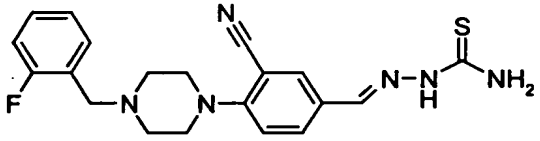
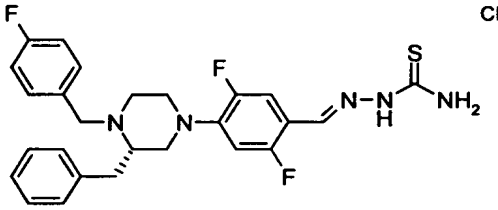
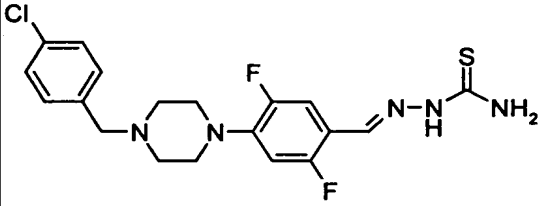
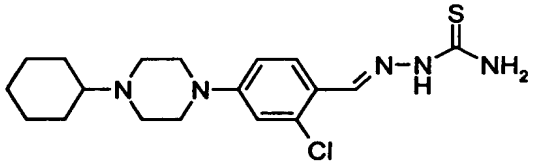
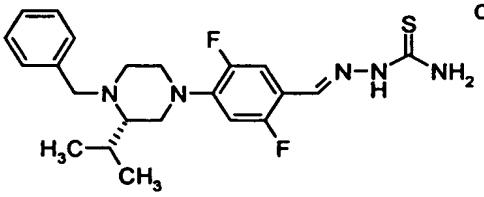
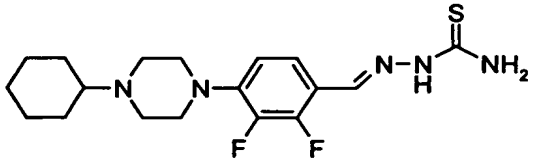
	Structure	Name	MH+
491		3-bromo-4-[4-(cyclohexylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	439
492		4-(4-benzyl-1,4-diazepan-1-yl)-3-chlorobenzaldehyde thiosemicarbazone	403
493		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-[4-(2-fluorobenzyl)piperazin-1-yl]benzonitrile	397
494		4-[(3S)-3-benzyl-4-(4-fluorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	499
495		4-[4-(4-chlorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	425
496		2-chloro-4-(4-cyclohexylpiperazin-1-yl)benzaldehyde thiosemicarbazone	381
497		4-[(3S)-4-benzyl-3-isopropylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	433
498		4-(4-cyclohexylpiperazin-1-yl)-2,3-difluorobenzaldehyde thiosemicarbazone	382

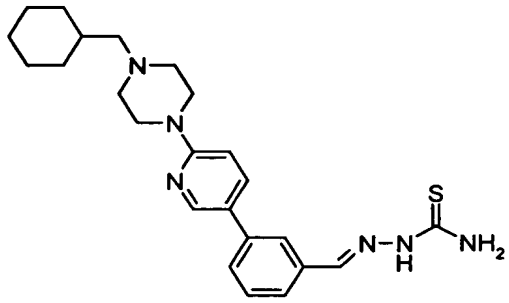
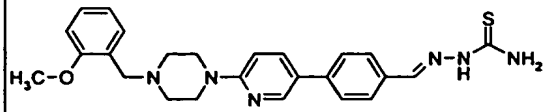
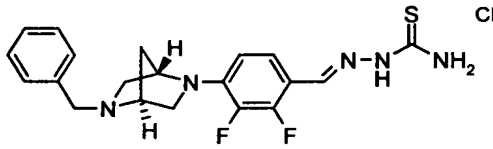
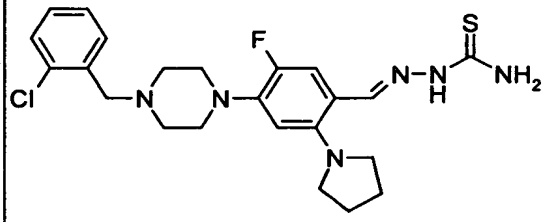
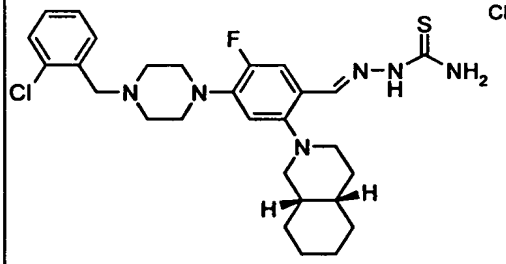
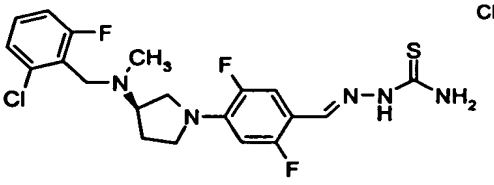
TABLE 3			
	Structure	Name	MH+
499		3-{6-[4-(cyclohexylmethyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	438
500		4-{6-[4-(2-methoxybenzyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	462
501	 Chiral	4-[(1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-2,3-difluorobenzaldehyde thiosemicarbazone	402
502		4-[4-(2-chlorobenzyl)piperazin-1-yl]-5-fluoro-2-pyrrolidin-1-ylbenzaldehyde thiosemicarbazone	476
503	 Chiral	4-[4-(2-chlorobenzyl)piperazin-1-yl]-5-fluoro-2-[(4aS,8aS)-octahydroisoquinolin-2(1H)-yl]benzaldehyde thiosemicarbazone	544
504	 Chiral	4-{(3R)-3-[(2-chloro-6-fluorobenzyl)(methyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	457

TABLE 3

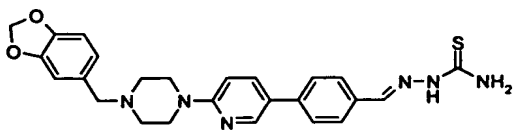
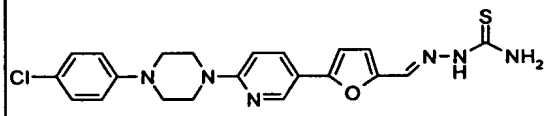
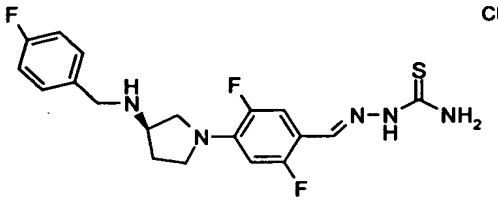
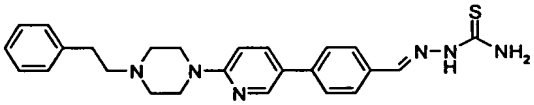
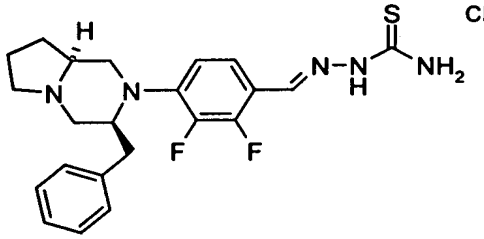
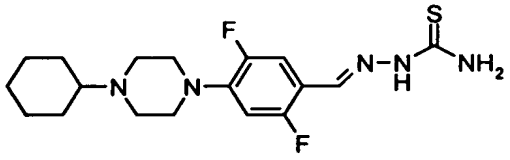
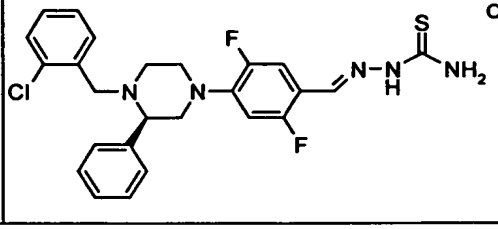
	Structure	Name	MH+
505		4-{6-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	476
506		5-{6-[4-(4-chlorophenyl)piperazin-1-yl]pyridin-3-yl}-2-furaldehyde thiosemicarbazone	442
507	 Chiral	2,5-difluoro-4-{(3R)-3-[(4-fluorobenzyl)amino]pyrrolidin-1-yl}benzaldehyde thiosemicarbazone	408
508		4-{6-[4-(2-phenylethyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	446
509	 Chiral	4-[(3S,8aS)-3-benzylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2,3-difluorobenzaldehyde thiosemicarbazone	431
510		4-(4-cyclohexylpiperazin-1-yl)-2,5-difluorobenzaldehyde thiosemicarbazone	382
511	 Chiral	4-[(3R)-4-(2-chlorobenzyl)-3-phenylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	501

TABLE 3

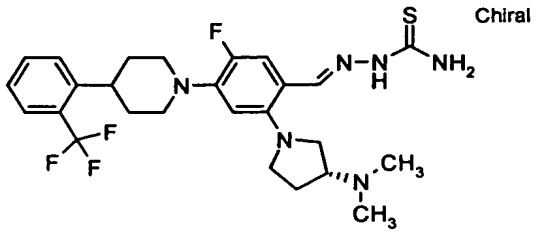
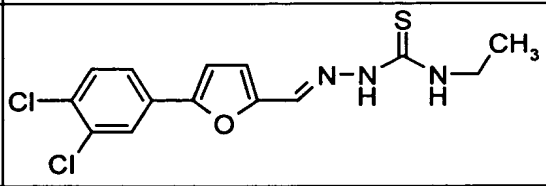
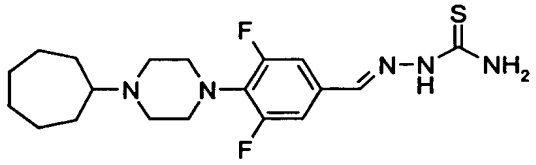
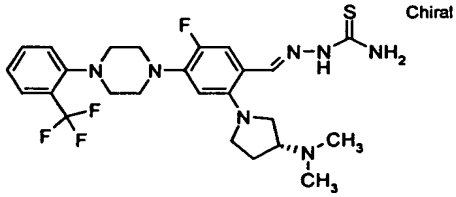
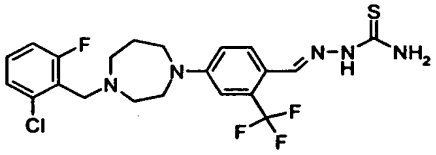
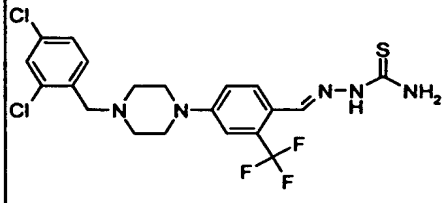
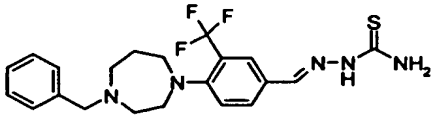
	Structure	Name	MH+
512	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-{4-[2-(trifluoromethyl)phenyl]piperidin-1-yl}benzaldehyde thiosemicarbazone	538
513		5-(3,4-dichlorophenyl)-2-furaldehyde N-ethylthiosemicarbazone	343
514		4-(4-cycloheptylpiperazin-1-yl)-3,5-difluorobenzaldehyde thiosemicarbazone	397
515	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-{4-[2-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	539
516		4-[4-(2-chloro-6-fluorobenzyl)-1,4-diazepan-1-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	489
517		4-[4-(2,4-dichlorobenzyl)piperazin-1-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	491
518		4-(4-benzyl-1,4-diazepan-1-yl)-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	437

TABLE 3

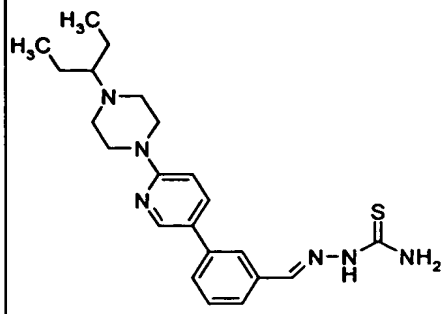
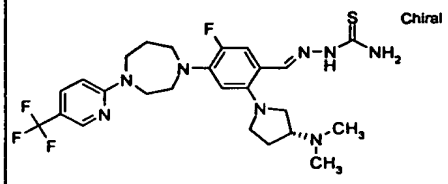
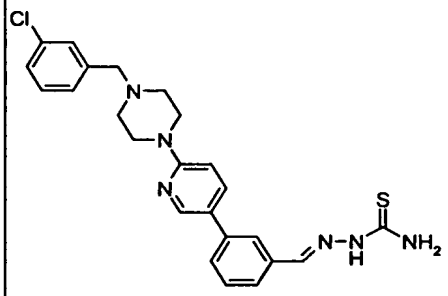
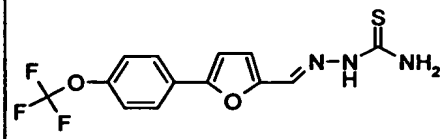
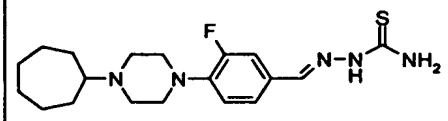
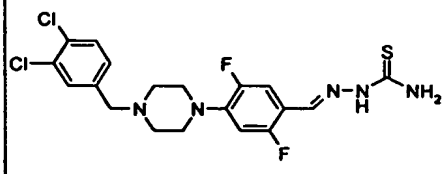
	Structur	Name	MH+
519		3-{6-[4-(1-ethylpropyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	412
520		2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-{4-[5-(trifluoromethyl)pyridin-2-yl]-1,4-diazepan-1-yl}benzaldehyde thiosemicarbazone	554
521		3-{6-[4-(3-chlorobenzyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	466
522		5-[4-(trifluoromethoxy)phenyl]-2-furaldehyde thiosemicarbazone	330
523		4-(4-cycloheptylpiperazin-1-yl)-3-fluorobenzaldehyde thiosemicarbazone	379
524		4-[4-(3,4-dichlorobenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	459

TABLE 3

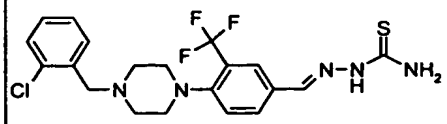
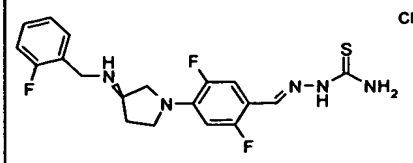
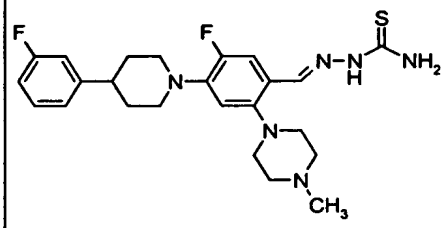
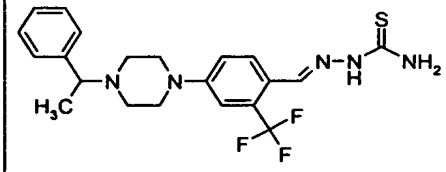
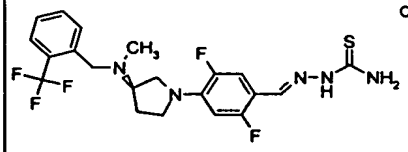
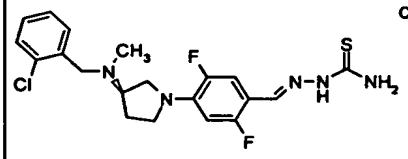
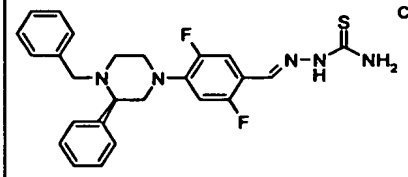
	Structure	Nam	MH+
525		4-[4-(2-chlorobenzyl)piperazin-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	457
526	 Chiral	2,5-difluoro-4-{(3R)-3-[(2-fluorobenzyl)amino]pyrrolidin-1-yl}benzaldehyde thiosemicarbazone	408
527		5-fluoro-4-[4-(3-fluorophenyl)piperidin-1-yl]-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	474
528		4-[4-(1-phenylethyl)piperazin-1-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	437
529	 Chiral	2,5-difluoro-4-((3R)-3-{methyl[2-(trifluoromethyl)benzyl]amino}pyrrolidin-1-yl)benzaldehyde thiosemicarbazone	472
530	 Chiral	4-{(3R)-3-[(2-chlorobenzyl)(methyl)amino]pyrrolidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	439
531	 Chiral	4-[(3R)-4-benzyl-3-phenylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	467

TABLE 3

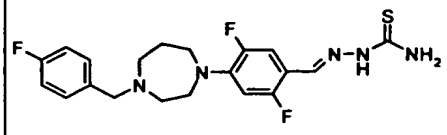
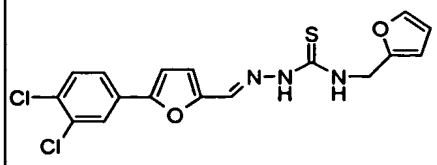
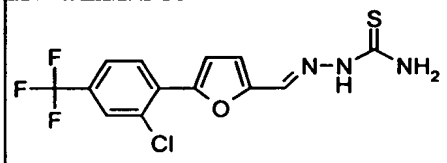
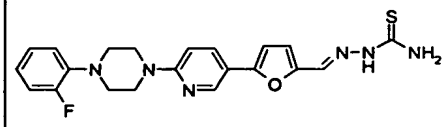
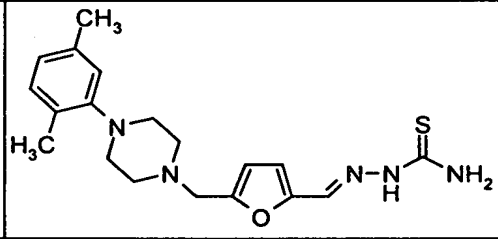
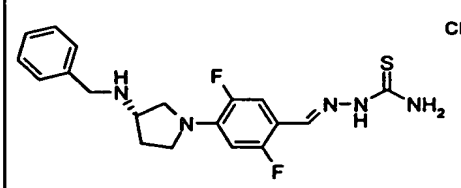
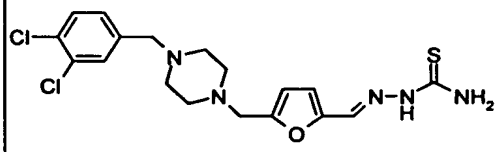
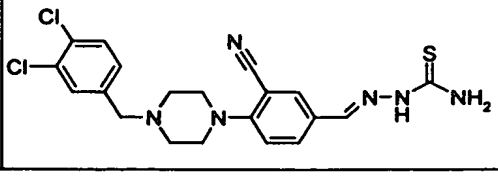
	Structure	Name	MH+
532		2,5-difluoro-4-[4-(4-fluorobenzyl)-1,4-diazepan-1-yl]benzaldehyde thiosemicarbazone	422
533		5-(3,4-dichlorophenyl)-2-furaldehyde N-(2-furylmethyl)thiosemicarbazone	395
534		5-[2-chloro-4-(trifluoromethyl)phenyl]-2-furaldehyde thiosemicarbazone	349
535		5-{6-[4-(2-fluorophenyl)piperazin-1-yl]pyridin-3-yl}-2-furaldehyde thiosemicarbazone	426
536		5-{[4-(2,5-dimethylphenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	373
537	 Chiral	4-[(3S)-3-(benzylamino)pyrrolidin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	390
538		5-{[4-(3,4-dichlorobenzyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	427
539		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-[4-(3,4-dichlorobenzyl)piperazin-1-yl]benzonitrile	448

TABLE 3

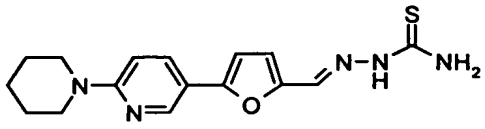
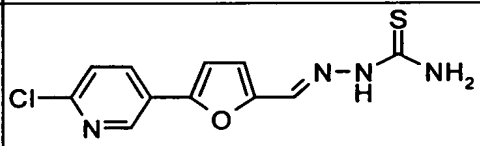
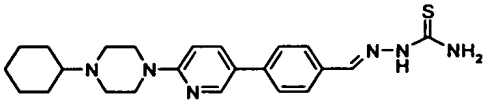
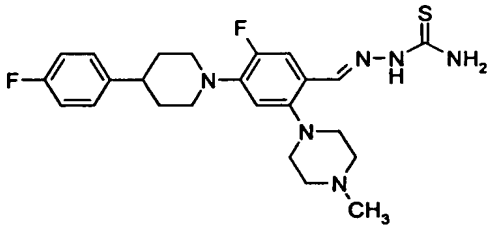
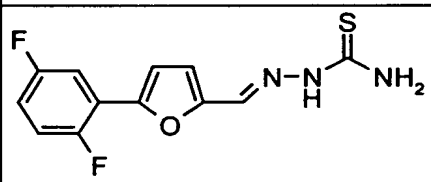
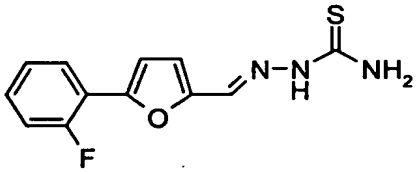
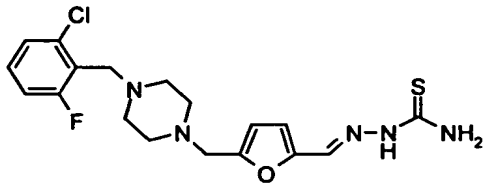
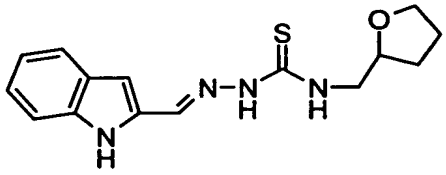
	Structur	Name	MH+
540		5-(6-piperidin-1-ylpyridin-3-yl)-2-furaldehyde thiosemicarbazone	330
541		5-(6-chloropyridin-3-yl)-2-furaldehyde thiosemicarbazone	282
542		4-[6-(4-cyclohexylpiperazin-1-yl)pyridin-3-yl]benzaldehyde thiosemicarbazone	424
543		5-fluoro-4-[4-(4-fluorophenyl)piperidin-1-yl]-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	474
544		5-(2,5-difluorophenyl)-2-furaldehyde thiosemicarbazone	282
545		5-(2-fluorophenyl)-2-furaldehyde thiosemicarbazone	264
546		5-{[4-(2-chloro-6-fluorobenzyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	411
547		1H-indole-2-carbaldehyde N-(tetrahydrofuran-2-ylmethyl)thiosemicarbazone	303

TABLE 3

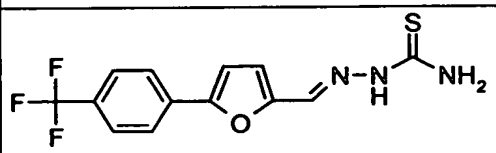
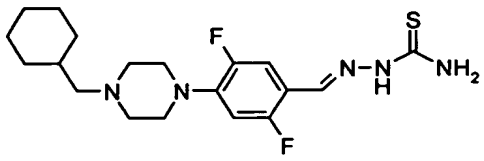
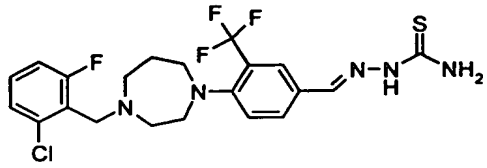
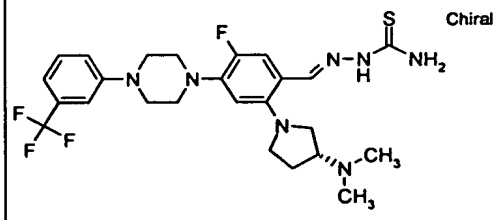
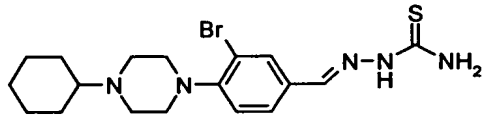
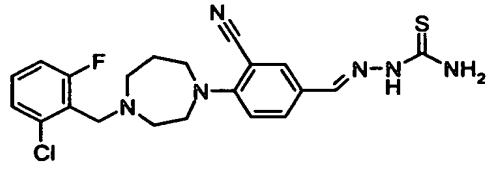
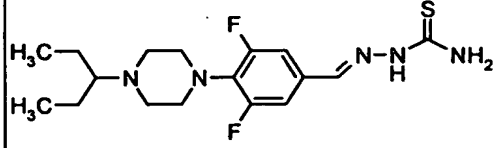
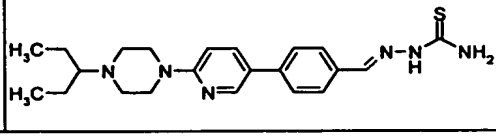
	Structur	Nam	MH+
548		5-[4-(trifluoromethyl)phenyl]-2-furaldehyde thiosemicarbazone	314
549		4-[4-(cyclohexylmethyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	397
550		4-[4-(2-chloro-6-fluorobenzyl)-1,4-diazepan-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	489
551		2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	539
552		3-bromo-4-(4-cyclohexylpiperazin-1-yl)benzaldehyde thiosemicarbazone	425
553		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-[4-(2-chloro-6-fluorobenzyl)-1,4-diazepan-1-yl]benzonitrile	446
554		4-[4-(1-ethylpropyl)piperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	370
555		4-{6-[4-(1-ethylpropyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	412

TABLE 3

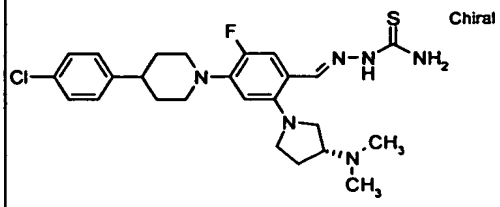
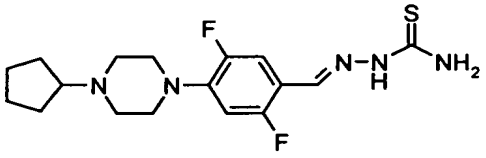
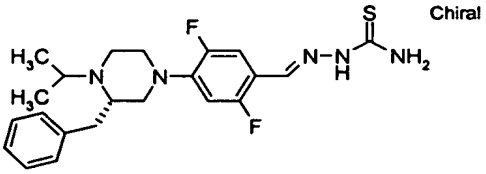
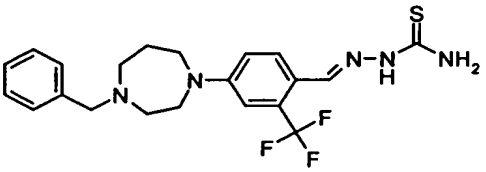
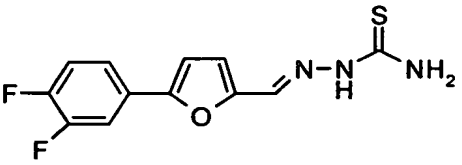
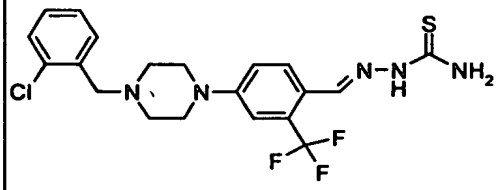
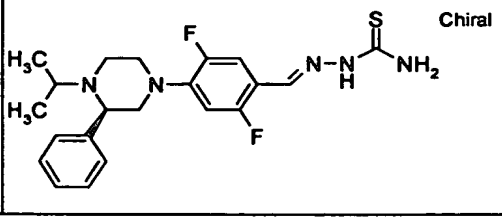
	Structure	Name	MH+
556	 Chiral	4-[4-(4-chlorophenyl)piperidin-1-yl]-2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	504
557		4-(4-cyclopentylpiperazin-1-yl)-2,5-difluorobenzaldehyde thiosemicarbazone	368
558	 Chiral	4-[(3S)-3-benzyl-4-isopropylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	433
559		4-(4-benzyl-1,4-diazepan-1-yl)-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	437
560		5-(3,4-difluorophenyl)-2-furaldehyde thiosemicarbazone	282
561		4-[4-(2-chlorobenzyl)piperazin-1-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	457
562	 Chiral	2,5-difluoro-4-[(3R)-4-isopropyl-3-phenylpiperazin-1-yl]benzaldehyde thiosemicarbazone	419

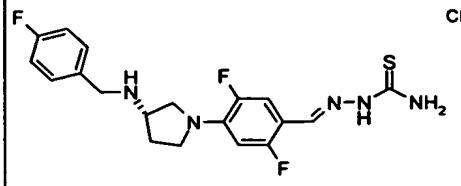
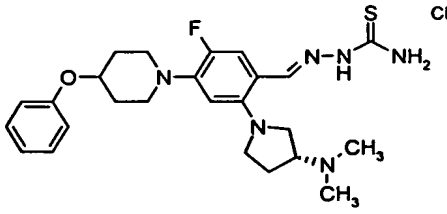
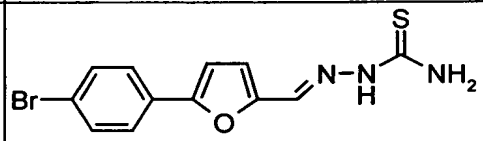
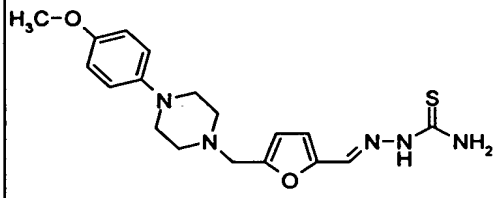
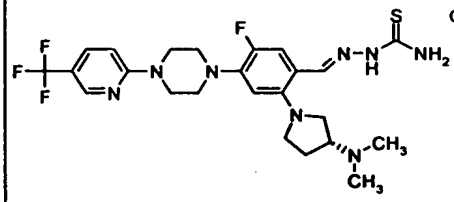
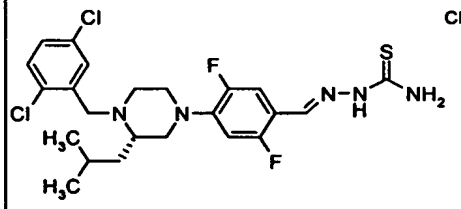
TABLE 3			
	Structure	Name	MH+
563	 Chiral	2,5-difluoro-4-{(3S)-3-[(4-fluorobenzyl)amino]pyrrolidin-1-yl}benzaldehyde thiosemicarbazone	408
564	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-(4-phenoxypiperidin-1-yl)benzaldehyde thiosemicarbazone	486
565		5-(4-bromophenyl)-2-furaldehyde thiosemicarbazone	325
566		5-{[4-(4-methoxyphenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	374
567	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-{4-[5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}benzaldehyde thiosemicarbazone	540
568	 Chiral	4-[(3S)-4-(2,5-dichlorobenzyl)-3-isobutylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	515

TABLE 3

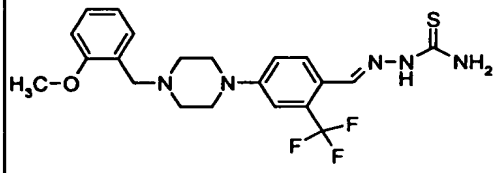
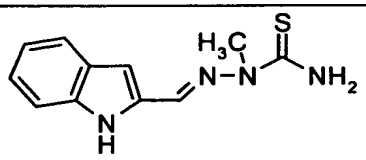
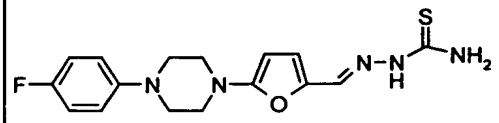
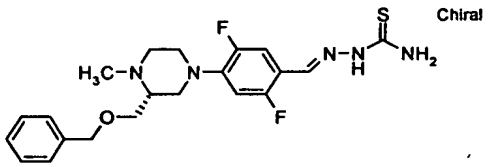
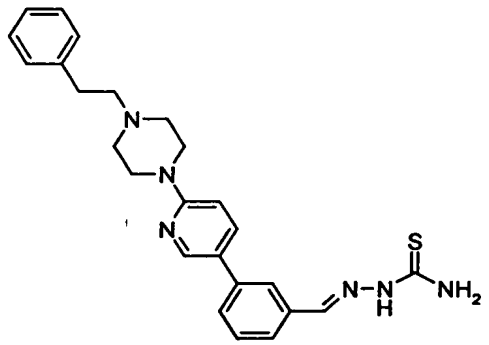
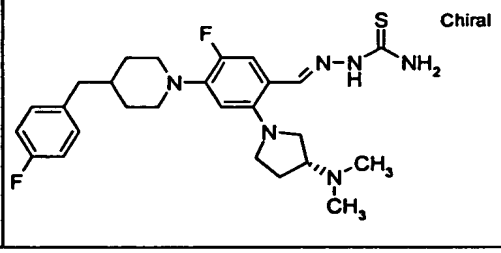
	Structure	Name	MH+
569		4-[4-(2-methoxybenzyl)piperazin-1-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	453
570		1H-indole-2-carbaldehyde N'-methylthiosemicarbazone	233
571		5-[4-(4-fluorophenyl)piperazin-1-yl]-2-furaldehyde thiosemicarbazone	348
572	 Chiral	4-{(3R)-3-[(benzyloxy)methyl]-4-methylpiperazin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	435
573		3-{6-[4-(2-phenylethyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	446
574	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-[4-(4-fluorobenzyl)piperidin-1-yl]benzaldehyde thiosemicarbazone	502

TABLE 3

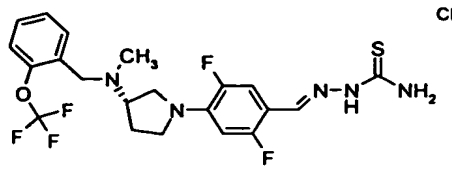
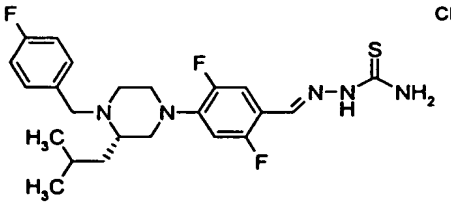
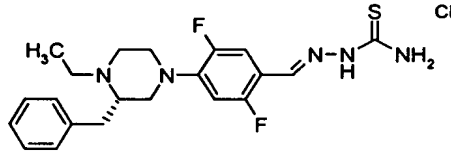
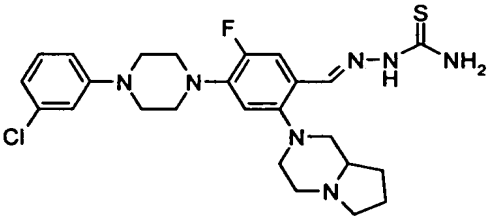
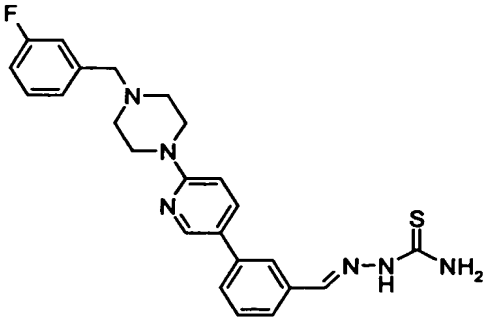
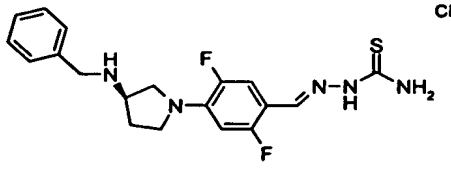
	Structur	Name	MH+
575	 Chiral	2,5-difluoro-4-((3S)-3-{methyl[2-(trifluoromethoxy)benzyl]amino}pyrrolidin-1-yl)benzaldehyde thiosemicarbazone	488
576	 Chiral	2,5-difluoro-4-[(3S)-4-(4-fluorobenzyl)-3-isobutylpiperazin-1-yl]benzaldehyde thiosemicarbazone	465
577	 Chiral	4-[(3S)-3-benzyl-4-ethylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	419
578		4-[4-(3-chlorophenyl)piperazin-1-yl]-5-fluoro-2-hexahydropyrrolo[1,2-a]pyrazin-2(1H)-ylbenzaldehyde thiosemicarbazone	517
579		3-{6-[4-(3-fluorobenzyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	450
580	 Chiral	4-[(3R)-3-(benzylamino)pyrrolidin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	390

TABLE 3

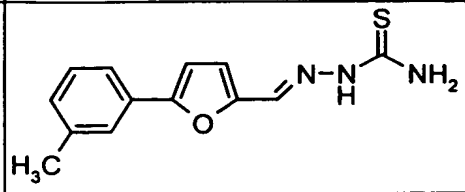
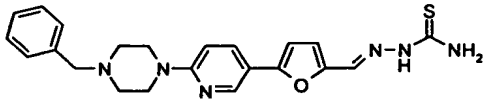
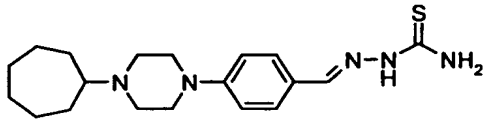
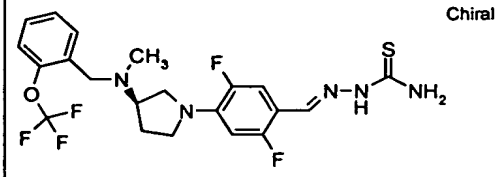
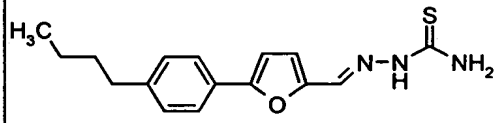
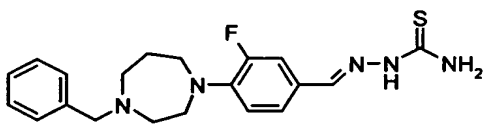
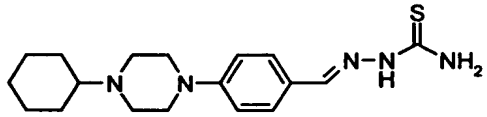
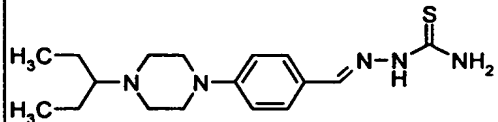
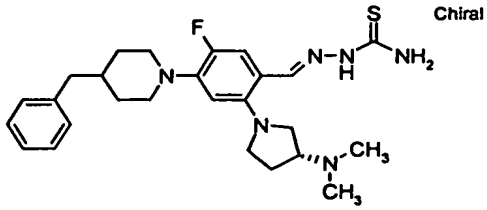
	Structure	Name	MH+
581		5-(3-methylphenyl)-2-furaldehyde thiosemicarbazone	260
582		5-[6-(4-benzylpiperazin-1-yl)pyridin-3-yl]-2-furaldehyde thiosemicarbazone	422
583		4-(4-cycloheptylpiperazin-1-yl)benzaldehyde thiosemicarbazone	361
584	 Chiral	2,5-difluoro-4-((3R)-3-{methyl[2-(trifluoromethoxy)benzyl]amino}pyrrolidin-1-yl)benzaldehyde thiosemicarbazone	488
585		5-(4-butylphenyl)-2-furaldehyde thiosemicarbazone	302
586		4-(4-benzyl-1,4-diazepan-1-yl)-3-fluorobenzaldehyde thiosemicarbazone	387
587		4-(4-cyclohexylpiperazin-1-yl)benzaldehyde thiosemicarbazone	347
588		4-[4-(1-ethylpropyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	335
589	 Chiral	4-(4-benzylpiperidin-1-yl)-2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	484

TABLE 3

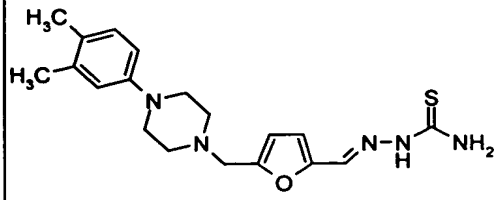
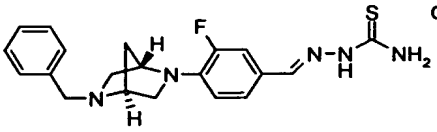
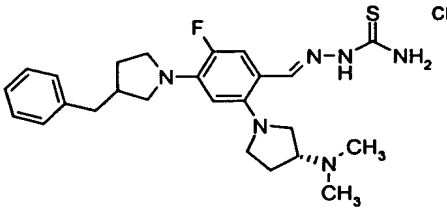
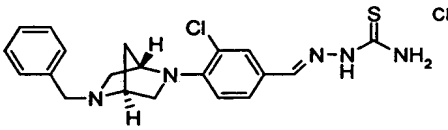
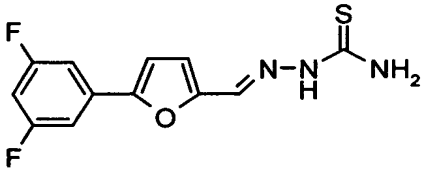
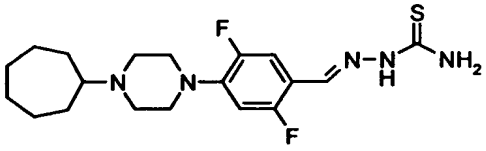
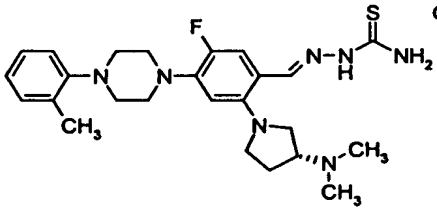
	Structure	Name	MH+
590		5-{[4-(3,4-dimethylphenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	373
591	 Chiral	4-[(1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-fluorobenzaldehyde thiosemicarbazone	384
592	 Chiral	4-(3-benzylpyrrolidin-1-yl)-2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	470
593	 Chiral	4-[(1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-chlorobenzaldehyde thiosemicarbazone	401
594		5-(3,5-difluorophenyl)-2-furaldehyde thiosemicarbazone	282
595		4-(4-cycloheptylpiperazin-1-yl)-2,5-difluorobenzaldehyde thiosemicarbazone	397
596	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-[4-(2-methylphenyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	485

TABLE 3

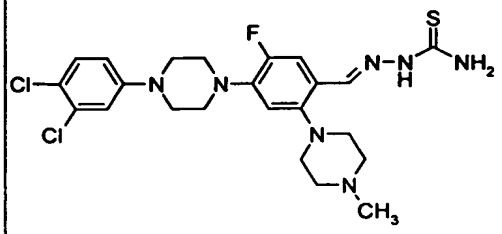
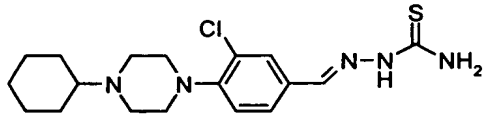
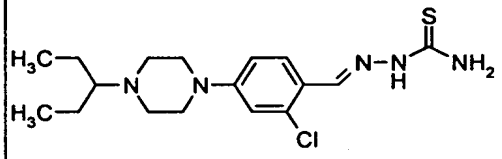
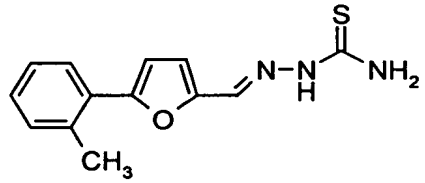
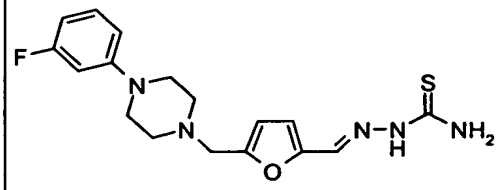
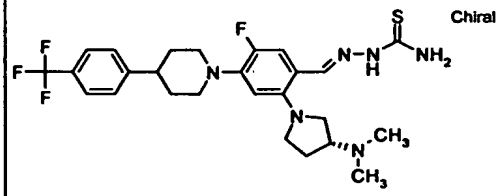
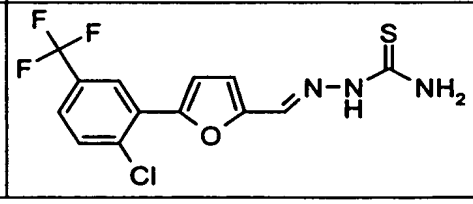
	Structur	Name	MH+
597		4-[4-(3,4-dichlorophenyl)piperazin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	525
598		3-chloro-4-(4-cyclohexylpiperazin-1-yl)benzaldehyde thiosemicarbazone	381
599		2-chloro-4-[4-(1-ethylpropyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	369
600		5-(2-methylphenyl)-2-furaldehyde thiosemicarbazone	260
601		5-{[4-(3-fluorophenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	362
602		2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-{4-[4-(trifluoromethyl)phenyl]piperidin-1-yl}benzaldehyde thiosemicarbazone	538
603		5-[2-chloro-5-(trifluoromethyl)phenyl]-2-furaldehyde thiosemicarbazone	349

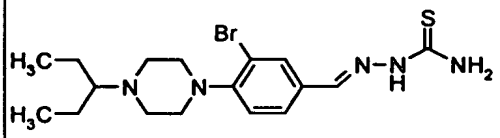
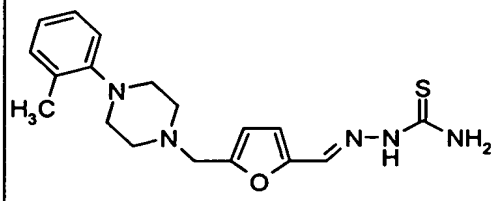
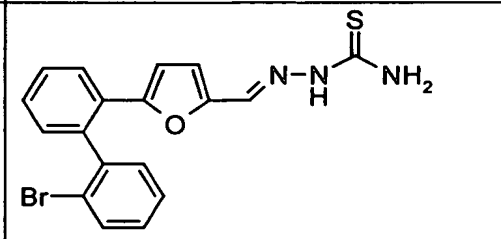
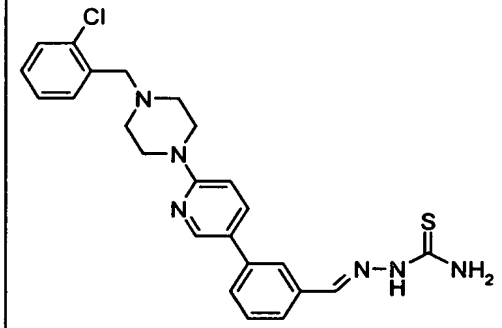
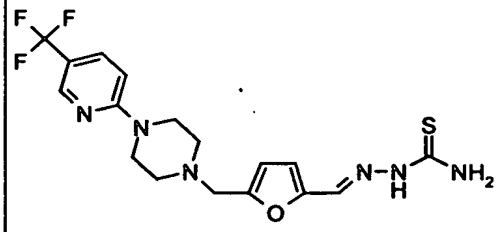
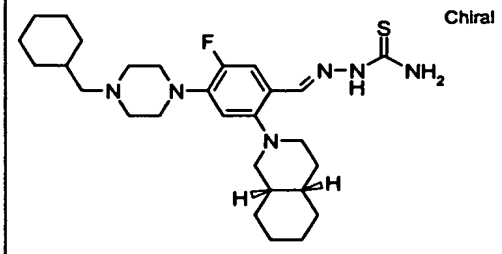
TABLE 3			
	Structur	Nam	MH+
604		3-bromo-4-[4-(1-ethylpropyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	413
605		5-{[4-(2-methylphenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	358
606		5-(2'-bromo-1,1'-biphenyl-2-yl)-2-furaldehyde thiosemicarbazone	401
607		3-{6-[4-(2-chlorobenzyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	466
608		5-({4-[5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}methyl)-2-furaldehyde thiosemicarbazone	413
609		4-[4-(cyclohexylmethyl)piperazin-1-yl]-5-fluoro-2-[(4aS,8aS)-octahydroisoquinolin-2(1H)-yl]benzaldehyde thiosemicarbazone	516

TABLE 3

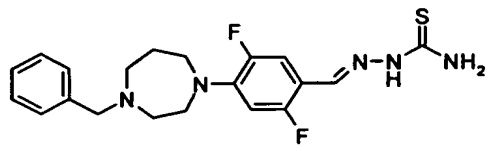
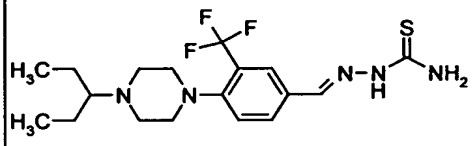
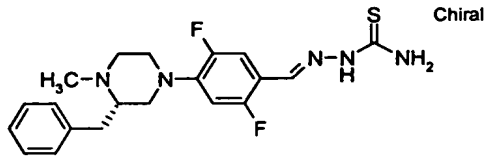
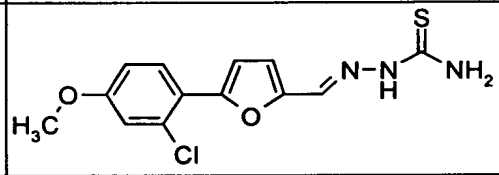
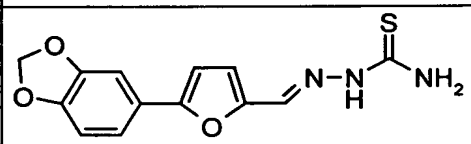
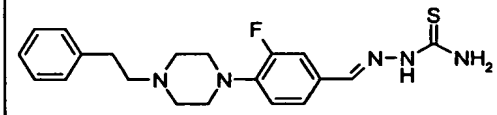
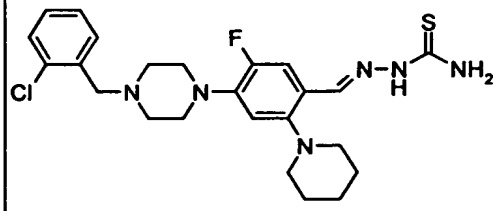
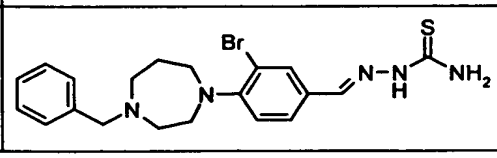
	Structure	Name	MH+
610		4-(4-benzyl-1,4-diazepan-1-yl)-2,5-difluorobenzaldehyde thiosemicarbazone	404
611		4-[4-(1-ethylpropyl)piperazin-1-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	402
612		4-[(3S)-3-benzyl-4-methylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	404
613		5-(2-chloro-4-methoxyphenyl)-2-furaldehyde thiosemicarbazone	311
614		5-(1,3-benzodioxol-5-yl)-2-furaldehyde thiosemicarbazone	290
615		3-fluoro-4-[4-(2-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	387
616		4-[4-(2-chlorobenzyl)piperazin-1-yl]-5-fluoro-2-piperidin-1-ylbenzaldehyde thiosemicarbazone	490
617		4-(4-benzyl-1,4-diazepan-1-yl)-3-bromobenzaldehyde thiosemicarbazone	447

TABLE 3

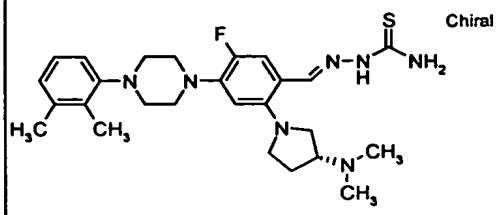
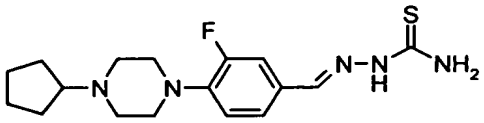
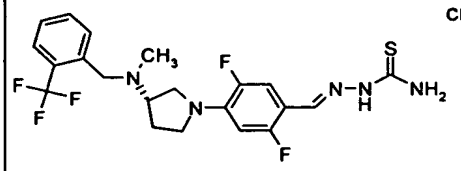
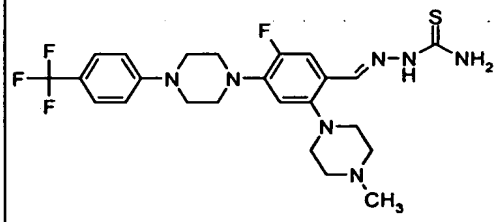
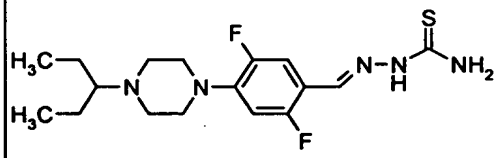
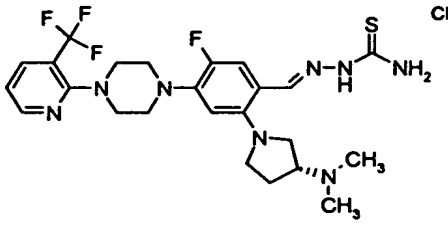
	Structure	Name	MH+
618	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-4-[4-(2,3-dimethylphenyl)piperazin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	499
619		4-(4-cyclopentylpiperazin-1-yl)-3-fluorobenzaldehyde thiosemicarbazone	350
620	 Chiral	2,5-difluoro-4-((3S)-3-{methyl[2-(trifluoromethyl)benzyl]amino}pyrrolidin-1-yl)benzaldehyde thiosemicarbazone	472
621		5-fluoro-2-(4-methylpiperazin-1-yl)-4-{4-[4-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	525
622		4-[4-(1-ethylpropyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	370
623	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-{4-[3-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}benzaldehyde thiosemicarbazone	540

TABLE 3

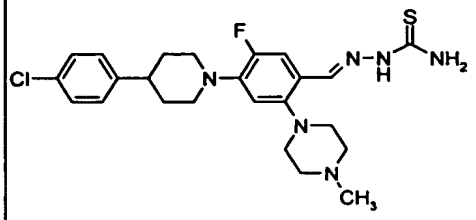
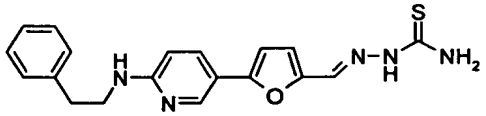
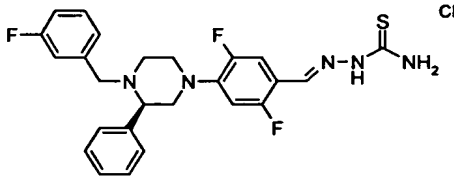
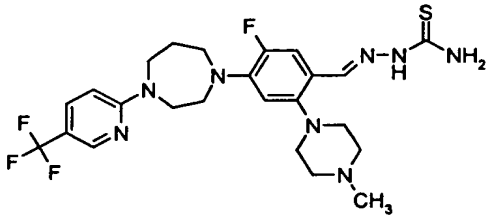
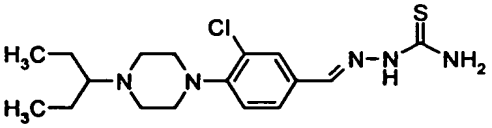
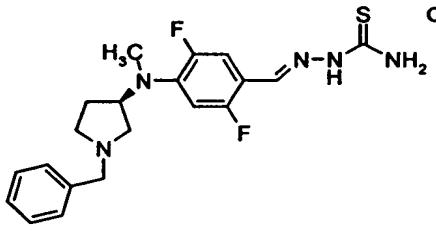
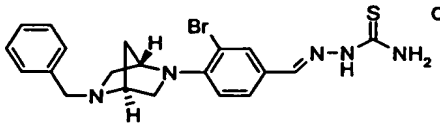
	Structure	Name	MH+
624		4-[4-(4-chlorophenyl)piperidin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	490
625		5-{6-[(2-phenylethyl)amino]pyridin-3-yl}-2-furaldehyde thiosemicarbazone	366
626	 Chiral	2,5-difluoro-4-[(3R)-4-(3-fluorobenzyl)-3-phenylpiperazin-1-yl]benzaldehyde thiosemicarbazone	485
627		5-fluoro-2-(4-methylpiperazin-1-yl)-4-{4-[5-(trifluoromethyl)pyridin-2-yl]-1,4-diazepan-1-yl}benzaldehyde thiosemicarbazone	540
628		3-chloro-4-[4-(1-ethylpropyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	369
629	 Chiral	4-[[(3R)-1-benzylpyrrolidin-3-yl](methyl)amino]-2,5-difluorobenzaldehyde thiosemicarbazone	404
630	 Chiral	4-[(1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-bromobenzaldehyde thiosemicarbazone	445

TABLE 3

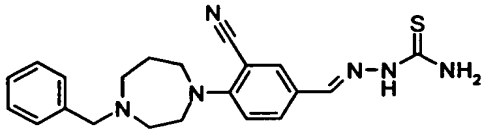
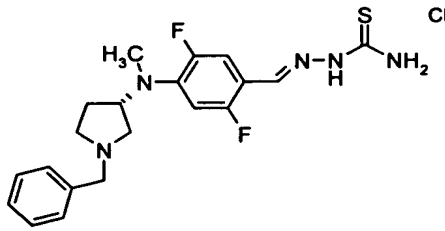
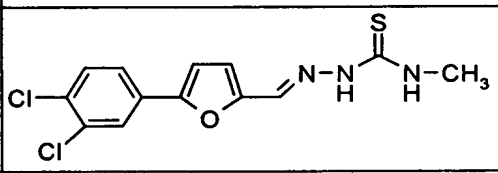
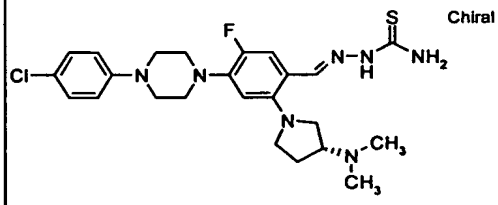
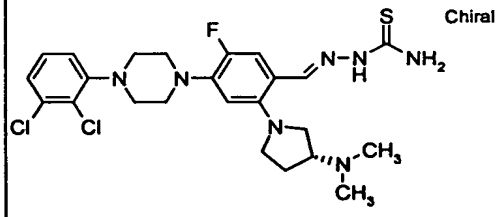
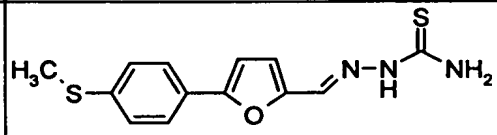
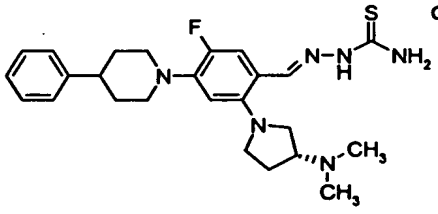
	Structure	Name	MH+
631		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-(4-benzyl-1,4-diazepan-1-yl)benzonitrile	394
632	 Chiral	4-[[(3S)-1-benzylpyrrolidin-3-yl](methyl)amino]-2,5-difluorobenzaldehyde thiosemicarbazone	404
633		5-(3,4-dichlorophenyl)-2-furaldehyde N-methylthiosemicarbazone	329
634	 Chiral	4-[4-(4-chlorophenyl)piperazin-1-yl]-2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	505
635	 Chiral	4-[4-(2,3-dichlorophenyl)piperazin-1-yl]-2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	540
636		5-[4-(methylthio)phenyl]-2-furaldehyde thiosemicarbazone	292
637	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-(4-phenylpiperidin-1-yl)benzaldehyde thiosemicarbazone	470

TABLE 3

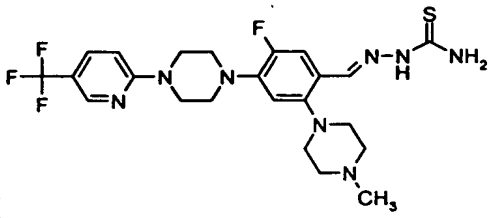
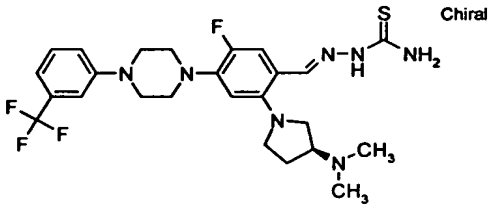
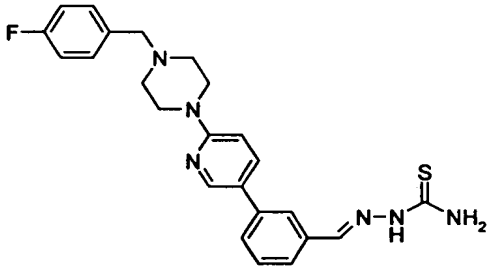
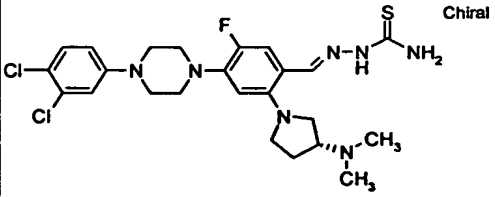
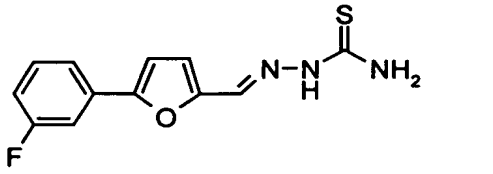
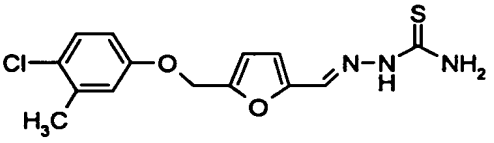
	Structure	Name	MH+
638		5-fluoro-2-(4-methylpiperazin-1-yl)-4-{4-[5-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}benzaldehyde thiosemicarbazone	526
639	 Chiral	2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	539
640		3-{6-[4-(4-fluorobenzyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	450
641	 Chiral	4-[4-(3,4-dichlorophenyl)piperazin-1-yl]-2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	540
642		5-(3-fluorophenyl)-2-furaldehyde thiosemicarbazone	264
643		5-[(4-chloro-3-methylphenoxy)methyl]-2-furaldehyde thiosemicarbazone	325

TABLE 3

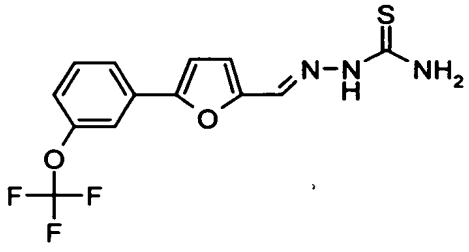
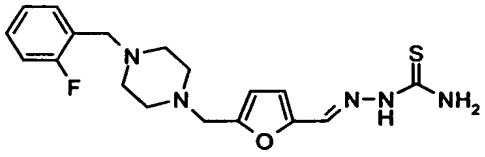
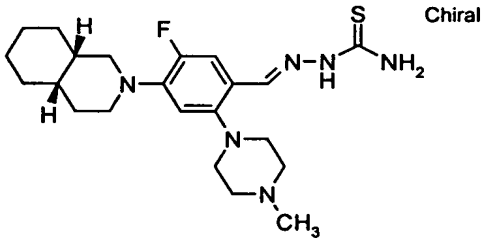
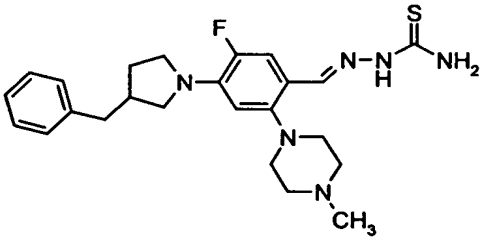
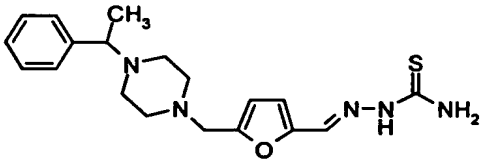
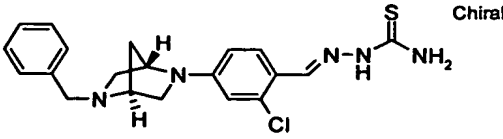
	Structur	Name	MH+
644		5-[3-(trifluoromethoxy)phenyl]-2-furaldehyde thiosemicarbazone	330
645		5-{[4-(2-fluorobenzyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	376
646	 Chiral	5-fluoro-2-(4-methylpiperazin-1-yl)-4-[(4aS,8aS)-octahydroisoquinolin-2(1H)-yl]benzaldehyde thiosemicarbazone	434
647		4-(3-benzylpyrrolidin-1-yl)-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	456
648		5-{[4-(1-phenylethyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	373
649	 Chiral	4-[(1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-2-chlorobenzaldehyde thiosemicarbazone	401

TABLE 3

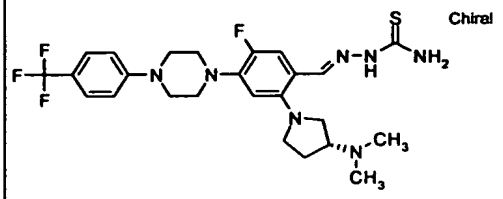
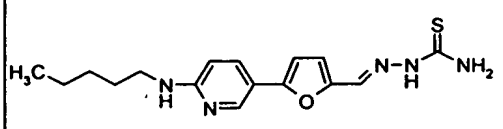
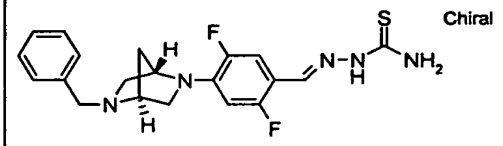
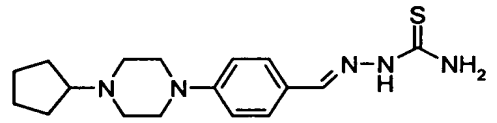
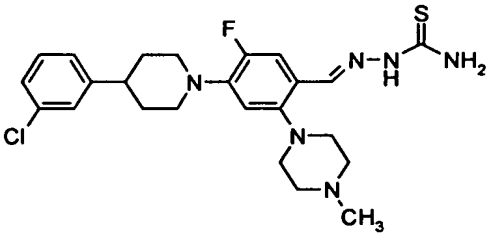
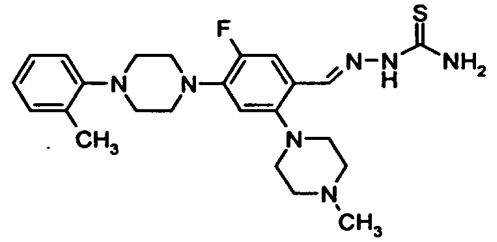
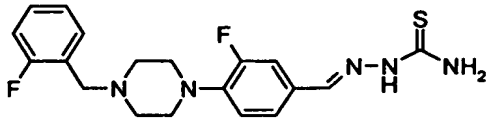
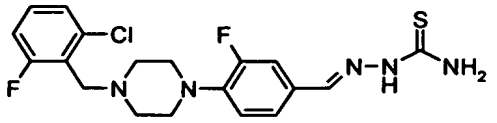
	Structure	Name	MH+
650	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-{4-[4-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	539
651		5-[6-(pentylamino)pyridin-3-yl]-2-furaldehyde thiosemicarbazone	332
652	 Chiral	4-[(1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	402
653		4-(4-cyclopentylpiperazin-1-yl)benzaldehyde thiosemicarbazone	332
654		4-[4-(3-chlorophenyl)piperidin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	490
655		5-fluoro-4-[4-(2-methylphenyl)piperazin-1-yl]-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	471
656		3-fluoro-4-[4-(2-fluorobenzyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	390
657		4-[4-(2-chloro-6-fluorobenzyl)piperazin-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	425

TABLE 3

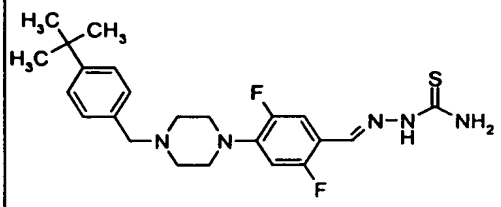
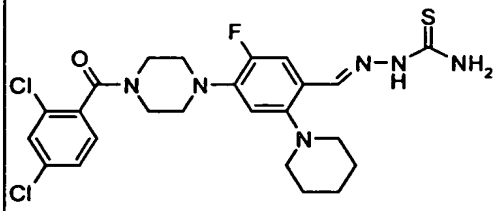
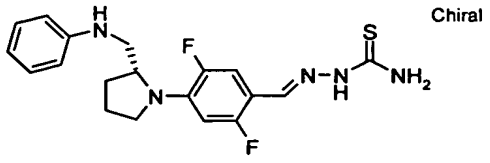
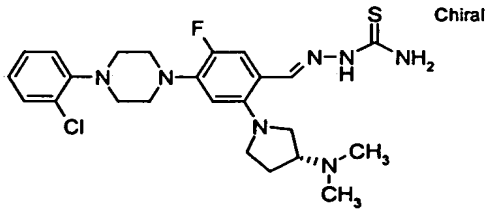
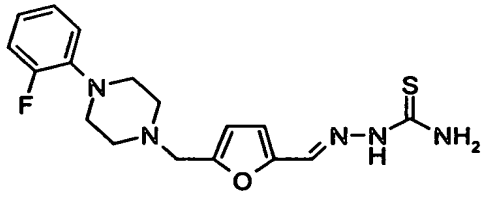
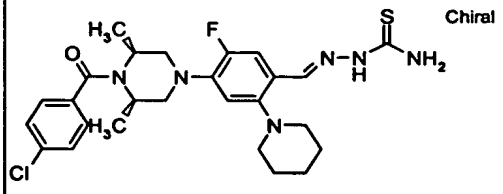
	Structure	Name	MH+
658		4-[4-(4-tert-butylbenzyl)piperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	447
659		4-[4-(2,4-dichlorobenzoyl)piperazin-1-yl]-5-fluoro-2-piperidin-1-ylbenzaldehyde thiosemicarbazone	538
660	 Chiral	4-[(2R)-2-(anilinomethyl)pyrrolidin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	390
661	 Chiral	4-[4-(2-chlorophenyl)piperazin-1-yl]-2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	505
662		5-{[4-(2-fluorophenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	362
663	 Chiral	4-[(3R,5S)-4-(4-chlorobenzoyl)-3,5-dimethylpiperazin-1-yl]-5-fluoro-2-piperidin-1-ylbenzaldehyde thiosemicarbazone	532

TABLE 3

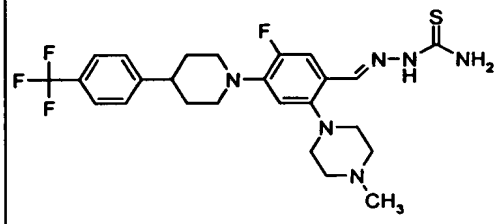
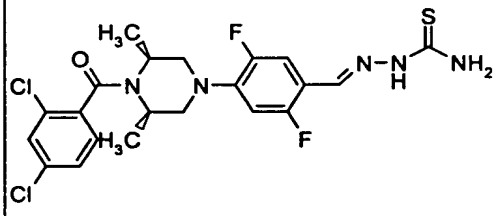
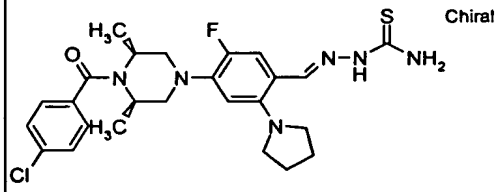
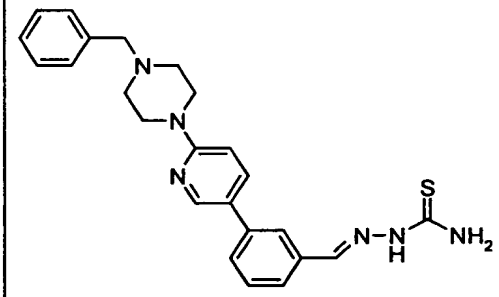
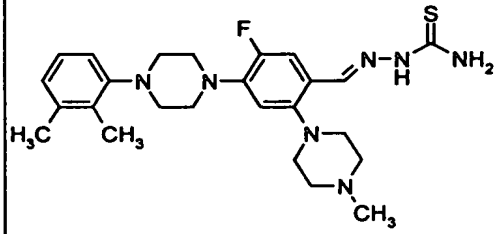
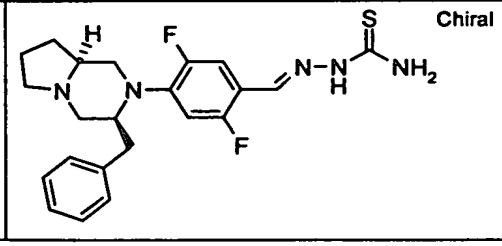
	Structure	Name	MH+
664		5-fluoro-2-(4-methylpiperazin-1-yl)-4-{4-[4-(trifluoromethyl)phenyl]piperidin-1-yl}benzaldehyde thiosemicarbazone	524
665		4-[(3R,5S)-4-(2,4-dichlorobenzoyl)-3,5-dimethylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	501
666	 Chiral	4-[(3R,5S)-4-(4-chlorobenzoyl)-3,5-dimethylpiperazin-1-yl]-5-fluoro-2-pyrrolidin-1-ylbenzaldehyde thiosemicarbazone	518
667		3-[6-(4-benzylpiperazin-1-yl)pyridin-3-yl]benzaldehyde thiosemicarbazone	432
668		4-[4-(2,3-dimethylphenyl)piperazin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	485
669	 Chiral	4-[(3S,8aS)-3-benzylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	431

TABLE 3

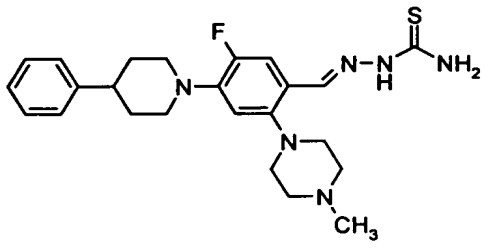
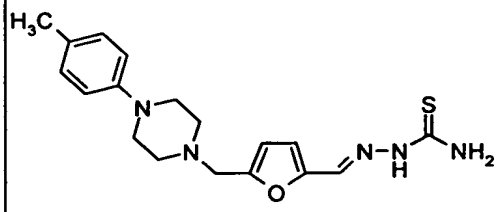
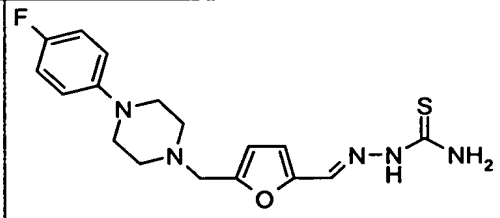
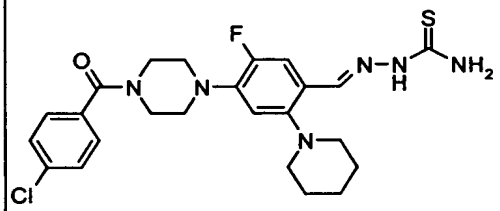
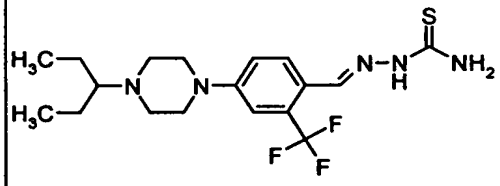
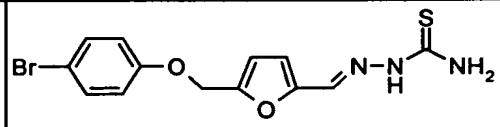
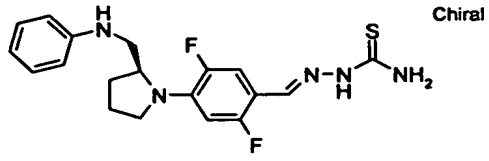
	Structure	Name	MH+
670		5-fluoro-2-(4-methylpiperazin-1-yl)-4-(4-phenylpiperidin-1-yl)benzaldehyde thiosemicarbazone	456
671		5-{[4-(4-methylphenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	358
672		5-{[4-(4-fluorophenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	362
673		4-[4-(4-chlorobenzoyl)piperazin-1-yl]-5-fluoro-2-piperidin-1-ylbenzaldehyde thiosemicarbazone	504
674		4-[4-(1-ethylpropyl)piperazin-1-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	402
675		5-[(4-bromophenoxy)methyl]-2-furaldehyde thiosemicarbazone	355
676		4-[(2S)-2-(anilinomethyl)pyrrolidin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	390

TABLE 3

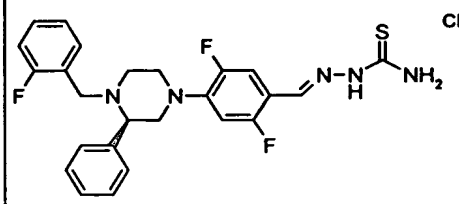
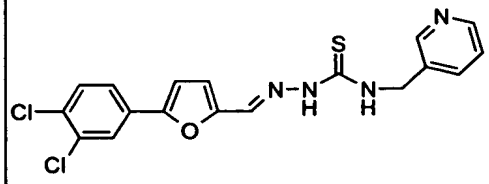
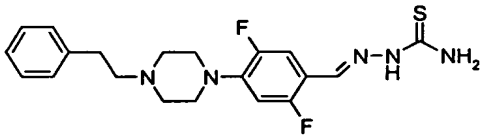
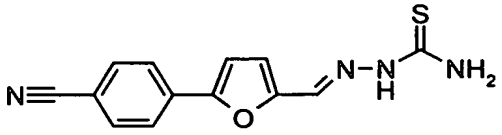
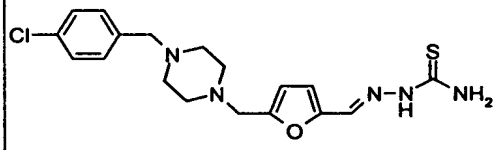
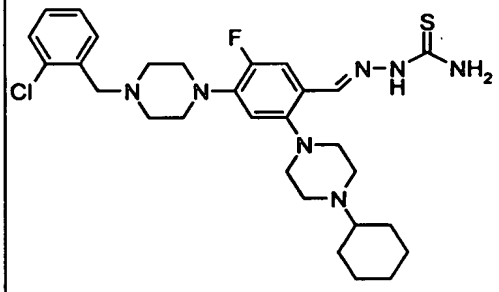
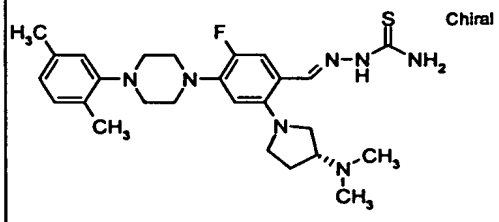
	Structure	Name	MH+
677	 Chiral	2,5-difluoro-4-[(3R)-4-(2-fluorobenzyl)-3-phenylpiperazin-1-yl]benzaldehyde thiosemicarbazone	485
678		5-(3,4-dichlorophenyl)-2-furaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone	406
679		2,5-difluoro-4-[4-(2-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	404
680		4-(5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-furyl)benzonitrile	271
681		5-{[4-(4-chlorobenzyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	393
682		4-[4-(2-chlorobenzyl)piperazin-1-yl]-2-(4-cyclohexylpiperazin-1-yl)-5-fluorobenzaldehyde thiosemicarbazone	573
683	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-4-[4-(2,5-dimethylphenyl)piperazin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	499

TABLE 3

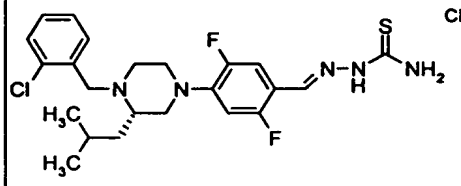
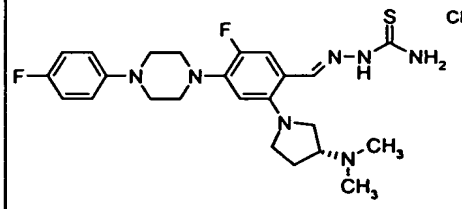
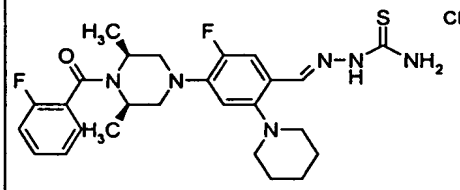
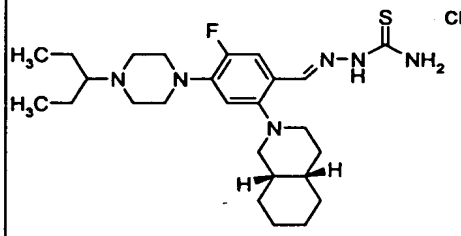
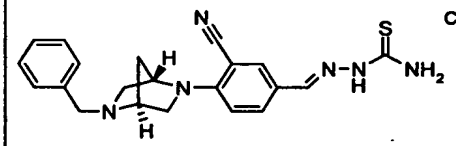
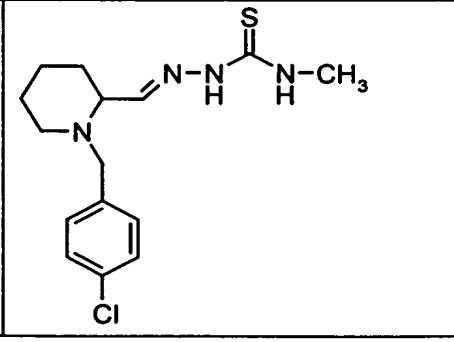
	Structure	Name	MH+
684	 Chiral	4-[(3S)-4-(2-chlorobenzyl)-3-isobutylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	481
685	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-[4-(4-fluorophenyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	489
686	 Chiral	5-fluoro-4-[(3R,5S)-4-(2-fluorobenzoyl)-3,5-dimethylpiperazin-1-yl]-2-piperidin-1-ylbenzaldehyde thiosemicarbazone	516
687	 Chiral	4-[4-(1-ethylpropyl)piperazin-1-yl]-5-fluoro-2-[(4aS,8aS)-octahydroisoquinolin-2(1H)-yl]benzaldehyde thiosemicarbazone	490
688	 Chiral	5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-[(1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]hept-2-yl]benzonitrile	392
689		1-(4-chlorobenzyl)piperidine-2-carbaldehyde N-methylthiosemicarbazone	326

TABLE 3

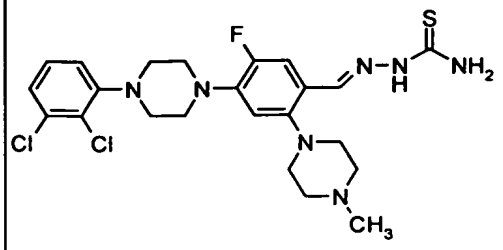
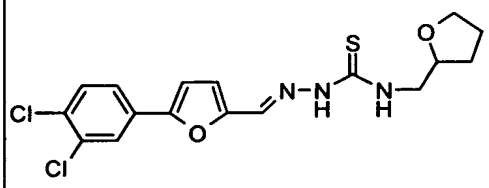
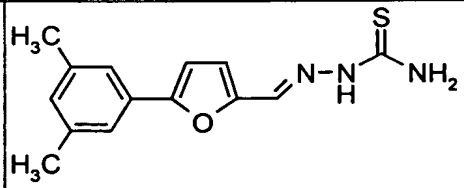
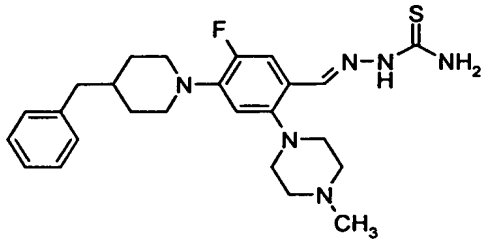
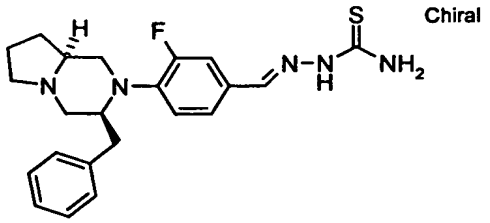
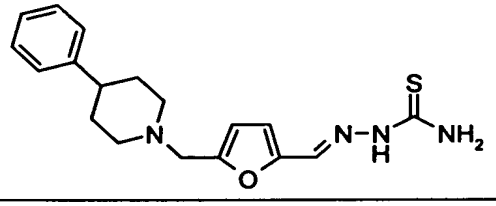
	Structure	Name	MH+
690		4-[4-(2,3-dichlorophenyl)piperazin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	525
691		5-(3,4-dichlorophenyl)-2-furaldehyde N-(tetrahydrofuran-2-ylmethyl)thiosemicarbazone	399
692		5-(3,5-dimethylphenyl)-2-furaldehyde thiosemicarbazone	274
693		4-(4-benzylpiperidin-1-yl)-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	470
694	 Chiral	4-[(3S,8aS)-3-benzylhexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl]-3-fluorobenzaldehyde thiosemicarbazone	413
695		5-[(4-phenylpiperidin-1-yl)methyl]-2-furaldehyde thiosemicarbazone	343

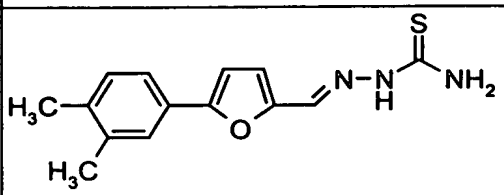
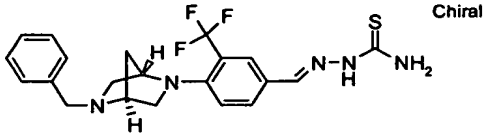
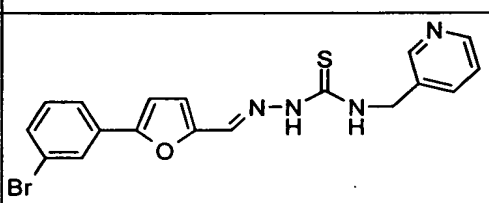
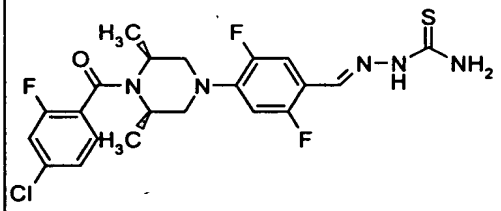
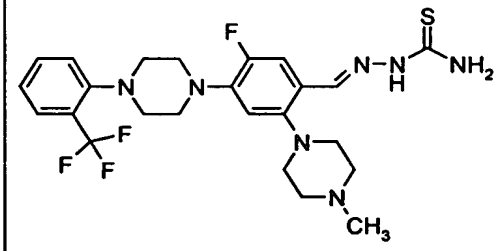
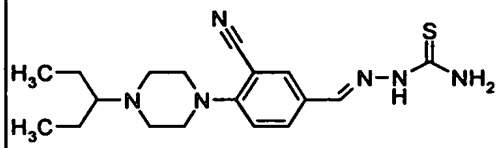
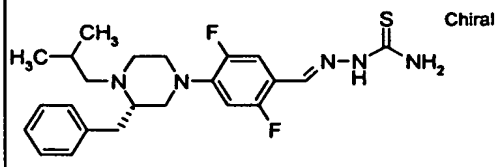
TABLE 3			
	Structure	Name	MH+
696		5-(3,4-dimethylphenyl)-2-furaldehyde thiosemicarbazone	274
697	 Chiral	4-[(1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-3-(trifluoromethyl)benzaldehyde thiosemicarbazone	435
698		5-(3-bromophenyl)-2-furaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone	416
699		4-[(3R,5S)-4-(4-chloro-2-fluorobenzoyl)-3,5-dimethylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	485
700		5-fluoro-2-(4-methylpiperazin-1-yl)-4-{4-[2-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	525
701		5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-[4-(1-ethylpropyl)piperazin-1-yl]benzonitrile	360
702	 Chiral	4-[(3S)-3-benzyl-4-isobutylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	447

TABLE 3

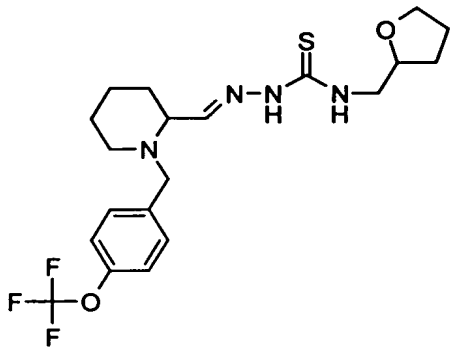
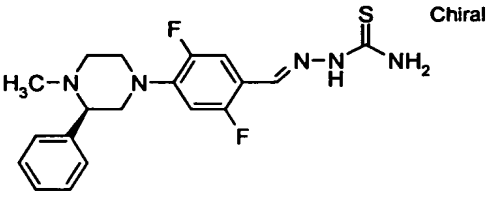
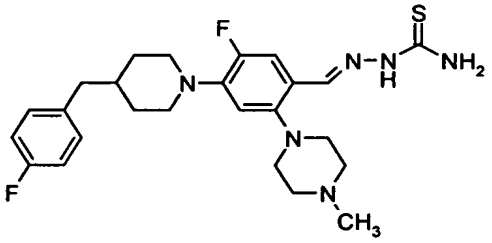
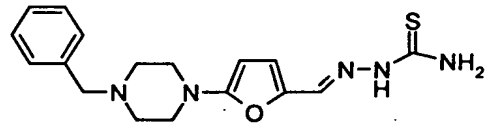
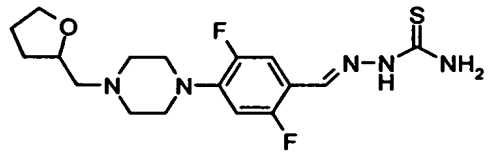
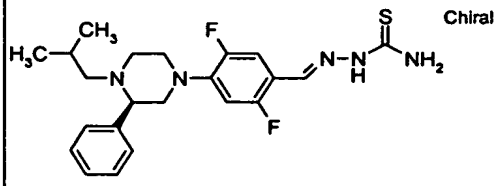
	Structure	Name	MH+
703		1-[4-(trifluoromethoxy)benzyl]piperidine-2-carbaldehyde N-(tetrahydrofuran-2-ylmethyl)thiosemicarbazone	446
704	 Chiral	2,5-difluoro-4-[(3R)-4-methyl-3-phenylpiperazin-1-yl]benzaldehyde thiosemicarbazone	390
705		5-fluoro-4-[4-(4-fluorobenzyl)piperidin-1-yl]-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	488
706		5-(4-benzylpiperazin-1-yl)-2-furaldehyde thiosemicarbazone	344
707		2,5-difluoro-4-[4-(tetrahydrofuran-2-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	384
708	 Chiral	2,5-difluoro-4-[(3R)-4-isobutyl-3-phenylpiperazin-1-yl]benzaldehyde thiosemicarbazone	433

TABLE 3

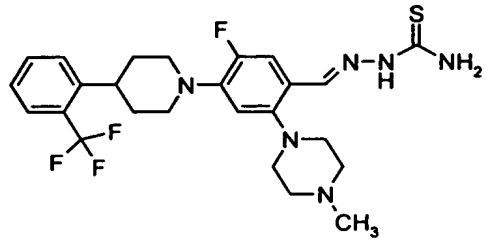
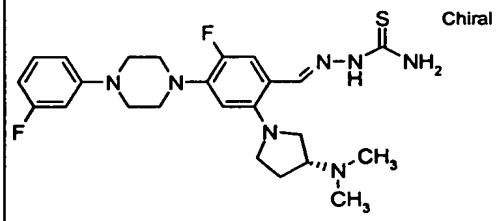
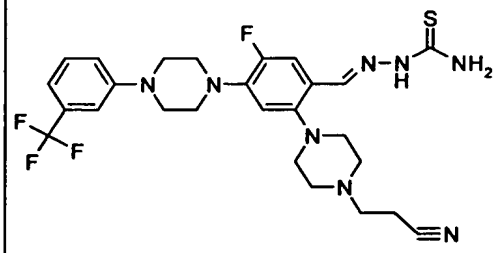
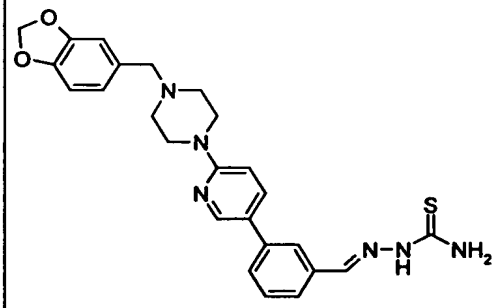
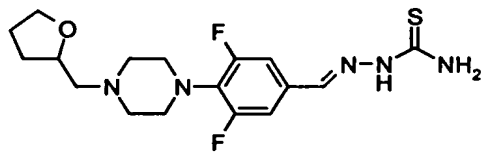
	Structure	Nam	MH+
709		5-fluoro-2-(4-methylpiperazin-1-yl)-4-{4-[2-(trifluoromethyl)phenyl]piperidin-1-yl}benzaldehyde thiosemicarbazone	524
710		2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-[4-(3-fluorophenyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	489
711		3-[4-(2-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-4-fluoro-5-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}phenyl)piperazin-1-yl]propanenitrile	564
712		3-{6-[4-(1,3-benzodioxol-5-ylmethyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	476
713		3,5-difluoro-4-[4-(tetrahydrofuran-2-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	384

TABLE 3

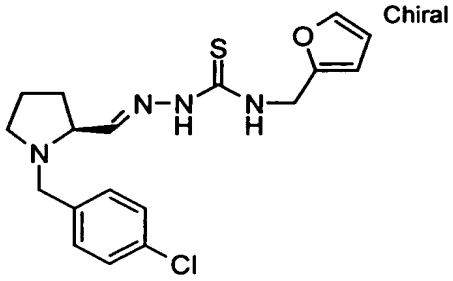
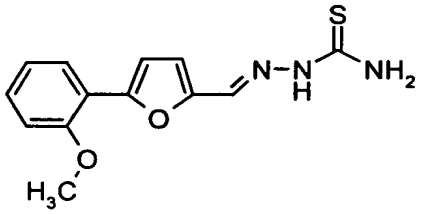
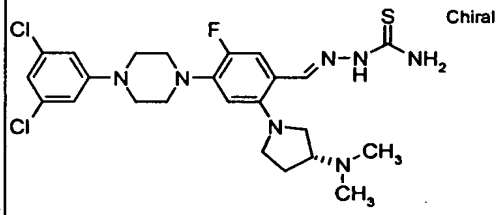
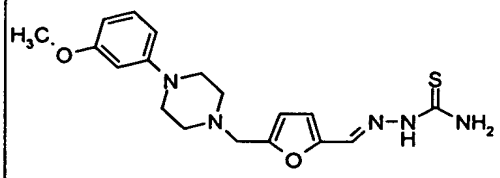
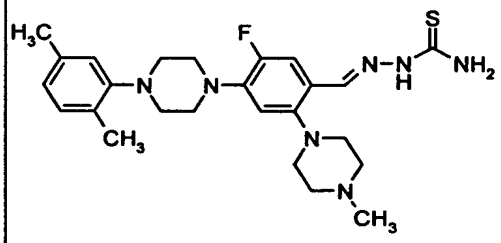
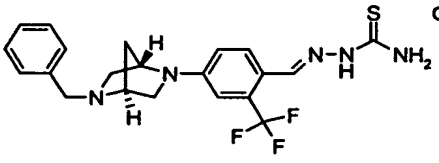
	Structure	Nam	MH+
714	 Chiral	(2S)-1-(4-chlorobenzyl)pyrrolidine-2-carbaldehyde N-(2-furylmethyl)thiosemicarbazone	378
715		5-(2-methoxyphenyl)-2-furaldehyde thiosemicarbazone	276
716	 Chiral	4-[4-(3,5-dichlorophenyl)piperazin-1-yl]-2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	540
717		5-{[4-(3-methoxyphenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	374
718		4-[4-(2,5-dimethylphenyl)piperazin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	485
719	 Chiral	4-[(1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]hept-2-yl]-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	435

TABLE 3

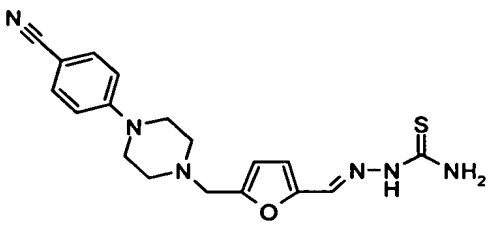
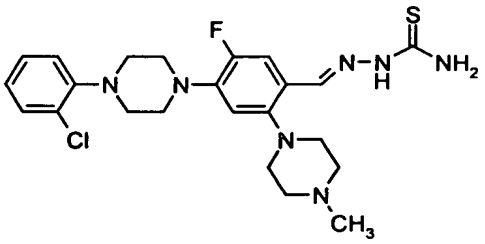
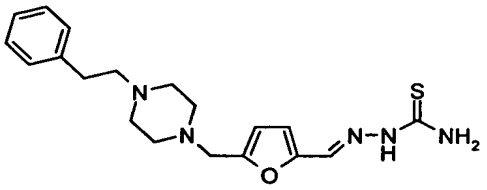
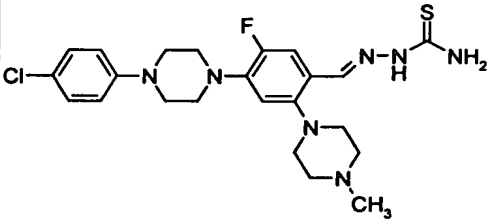
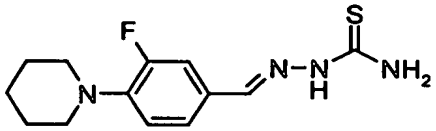
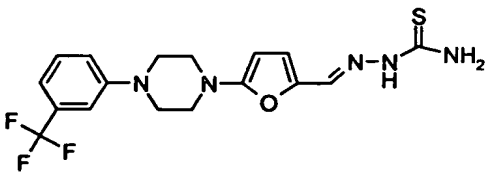
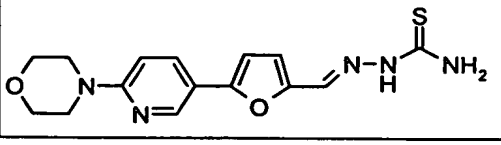
	Structure	Name	MH+
720		4-{4-[(5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-furyl)methyl]piperazin-1-yl}benzonitrile	369
721		4-[4-(2-chlorophenyl)piperazin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	491
722		5-{[4-(2-phenylethyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	373
723		4-[4-(4-chlorophenyl)piperazin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	491
724		3-fluoro-4-piperidin-1-ylbenzaldehyde thiosemicarbazone	281
725		5-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}-2-furaldehyde thiosemicarbazone	398
726		5-(6-morpholin-4-ylpyridin-3-yl)-2-furaldehyde thiosemicarbazone	332

TABLE 3

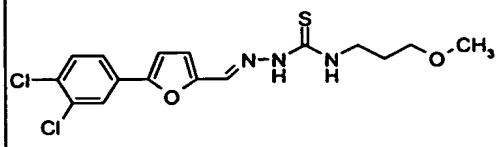
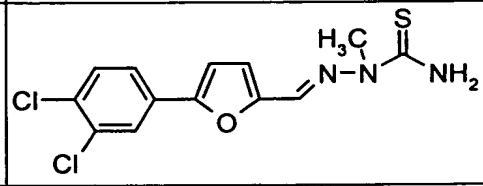
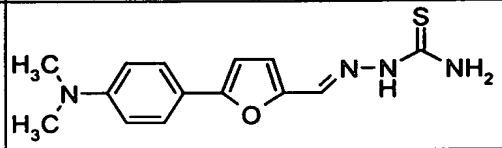
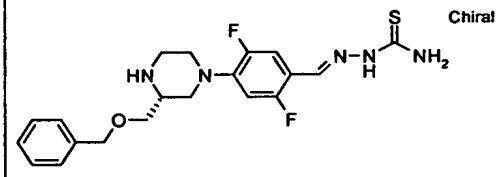
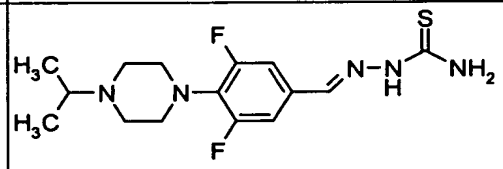
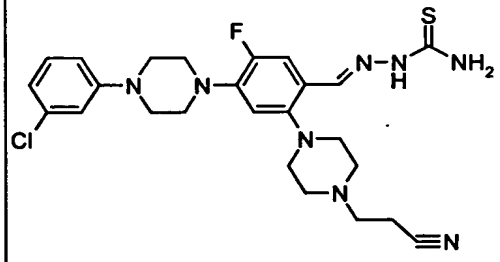
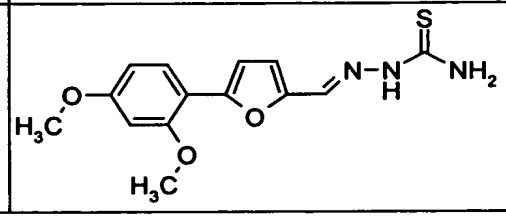
	Structur	Name	MH+
727		5-(3,4-dichlorophenyl)-2-furaldehyde N-(3-methoxypropyl)thiosemicarbazone	387
728		5-(3,4-dichlorophenyl)-2-furaldehyde N'-methylthiosemicarbazone	329
729		5-[4-(dimethylamino)phenyl]-2-furaldehyde thiosemicarbazone	289
730		4-{(3R)-3-[(benzyloxy)methyl]piperazin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	420
731		3,5-difluoro-4-(4-isopropylpiperazin-1-yl)benzaldehyde thiosemicarbazone	342
732		3-(4-{2-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-5-[4-(3-chlorophenyl)piperazin-1-yl]-4-fluorophenyl}piperazin-1-yl)propanenitrile	530
733		5-(2,4-dimethoxyphenyl)-2-furaldehyde thiosemicarbazone	306

TABLE 3

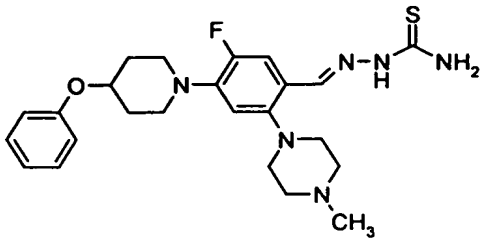
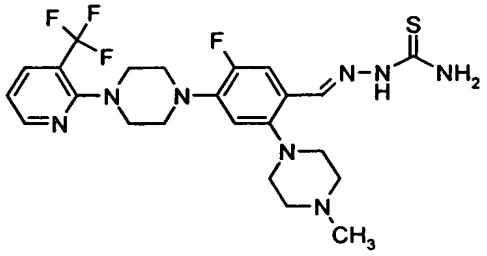
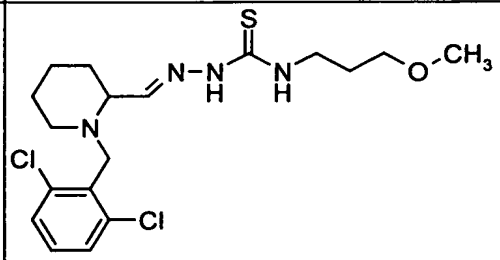
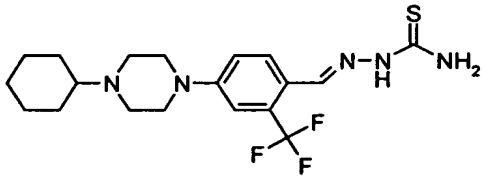
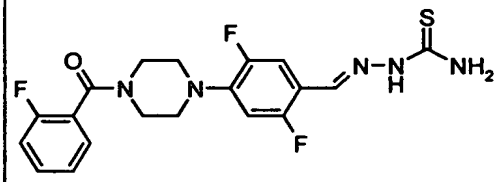
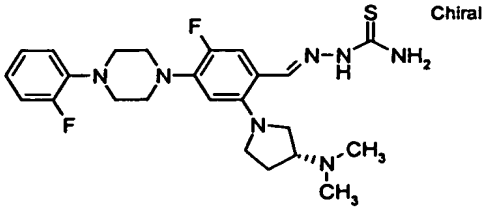
	Structure	Name	MH+
734		5-fluoro-2-(4-methylpiperazin-1-yl)-4-(4-phenoxypiperidin-1-yl)benzaldehyde thiosemicarbazone	472
735		5-fluoro-2-(4-methylpiperazin-1-yl)-4-{4-[3-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl}benzaldehyde thiosemicarbazone	526
736		1-(2,6-dichlorobenzyl)piperidine-2-carbaldehyde N-(3-methoxypropyl)thiosemicarbazone	418
737		4-(4-cyclohexylpiperazin-1-yl)-2-(trifluoromethyl)benzaldehyde thiosemicarbazone	415
738		2,5-difluoro-4-[4-(2-fluorobenzoyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	422
739	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-[4-(2-fluorophenyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	489

TABLE 3

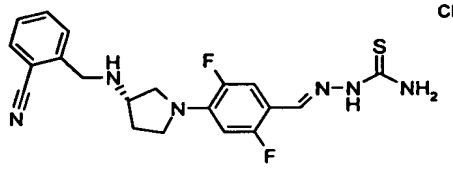
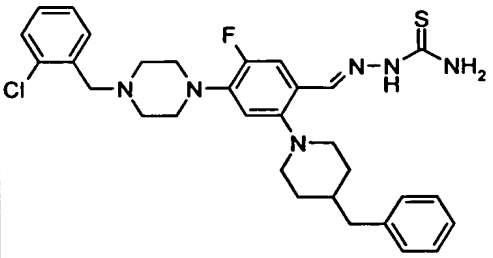
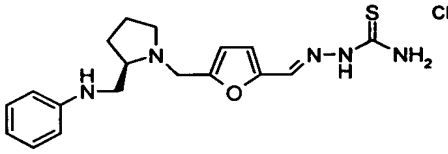
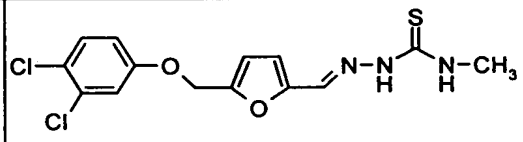
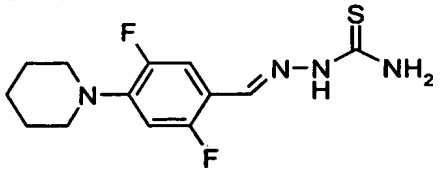
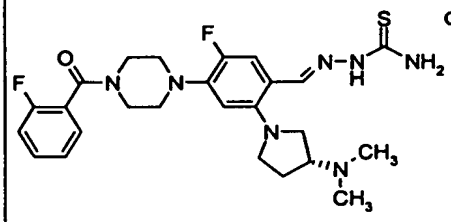
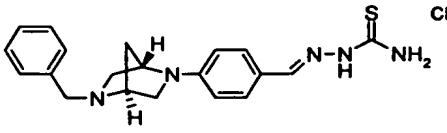
	Structure	Nam	MH+
740	 Chiral	2-({[(3S)-1-(4-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2,5-difluorophenyl)pyrrolidin-3-yl]amino}methyl)benzonitrile	415
741		2-(4-benzylpiperidin-1-yl)-4-[4-(2-chlorobenzyl)piperazin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	580
742	 Chiral	5-{[(2R)-2-(anilinomethyl)pyrrolidin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	358
743		5-[(3,4-dichlorophenoxy)methyl]-2-furaldehyde N-methylthiosemicarbazone	359
744		2,5-difluoro-4-piperidin-1-ylbenzaldehyde thiosemicarbazone	299
745	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-[4-(2-fluorobenzoyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	517
746	 Chiral	4-[(1S,4S)-5-benzyl-2,5-diazabicyclo[2.2.1]hept-2-yl]benzaldehyde thiosemicarbazone	367

TABLE 3

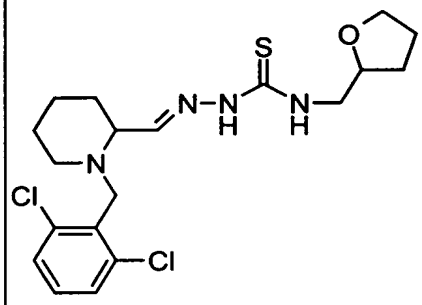
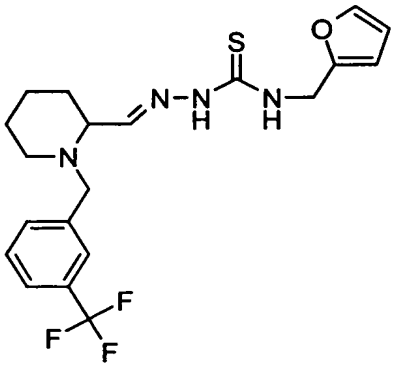
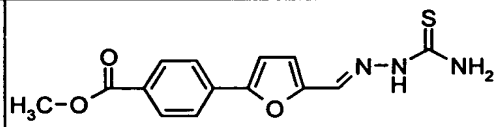
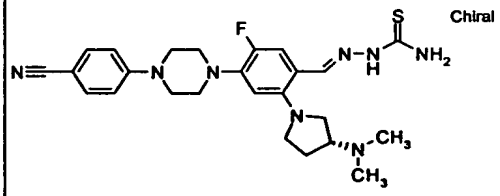
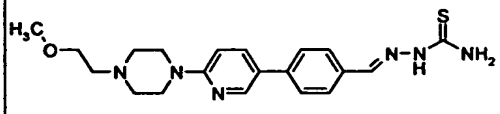
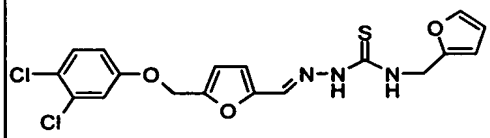
	Structure	Name	MH+
747		1-(2,6-dichlorobenzyl)piperidine-2-carbaldehyde N-(tetrahydrofuran-2-ylmethyl)thiosemicarbazone	430
748		1-[3-(trifluoromethyl)benzyl]piperidine-2-carbaldehyde N-(2-furylmethyl)thiosemicarbazone	425
749		methyl 4-(5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-furyl)benzoate	304
750		4-(4-{4-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-5-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-fluorophenyl}piperazin-1-yl)benzonitrile	496
751		4-{6-[4-(2-methoxyethyl)piperazin-1-yl]pyridin-3-yl}benzaldehyde thiosemicarbazone	400
752		5-[(3,4-dichlorophenoxy)methyl]-2-furaldehyde N-(2-furylmethyl)thiosemicarbazone	425

TABLE 3

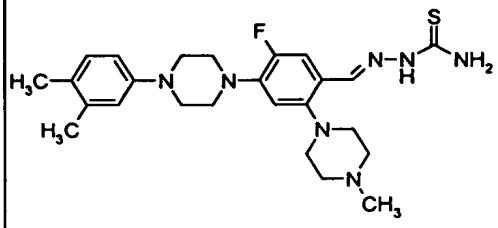
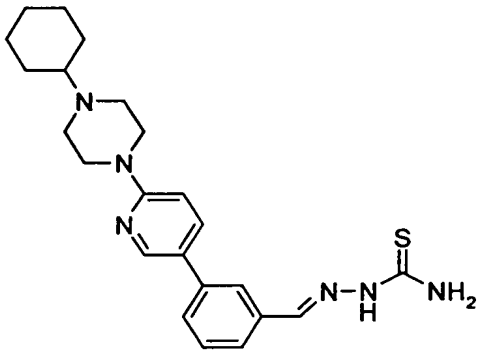
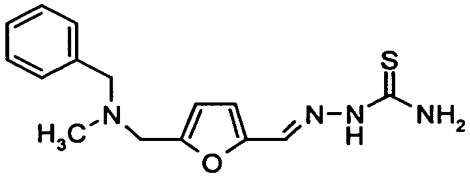
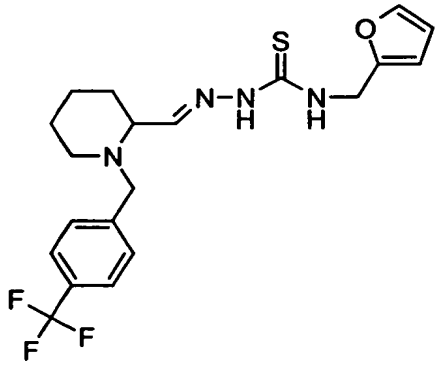
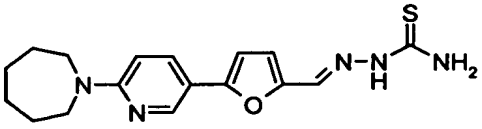
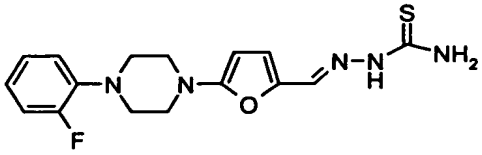
	Structure	Name	MH+
753		4-[4-(3,4-dimethylphenyl)piperazin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	485
754		3-[6-(4-cyclohexylpiperazin-1-yl)pyridin-3-yl]benzaldehyde thiosemicarbazone	424
755		5-{[benzyl(methyl)amino]methyl}-2-furaldehyde thiosemicarbazone	303
756		1-[4-(trifluoromethyl)benzyl]piperidine-2-carbaldehyde N-(2-furylmethyl)thiosemicarbazone	425
757		5-(6-azepan-1-ylpyridin-3-yl)-2-furaldehyde thiosemicarbazone	344
758		5-[4-(2-fluorophenyl)piperazin-1-yl]-2-furaldehyde thiosemicarbazone	348

TABLE 3

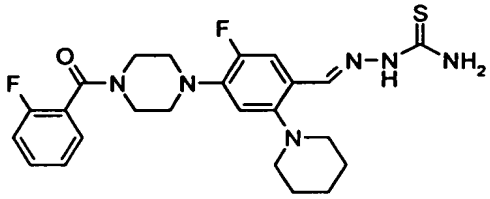
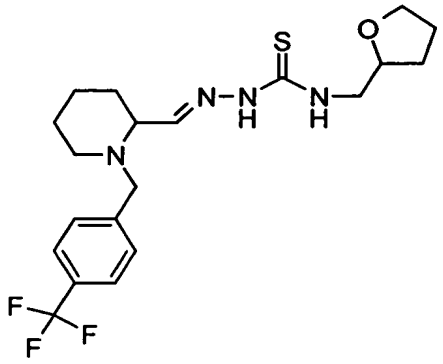
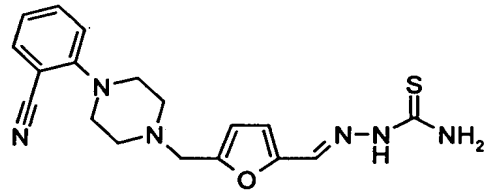
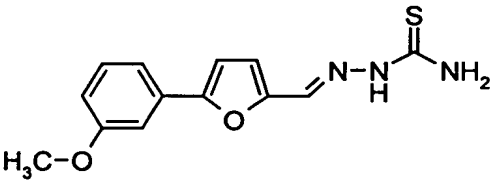
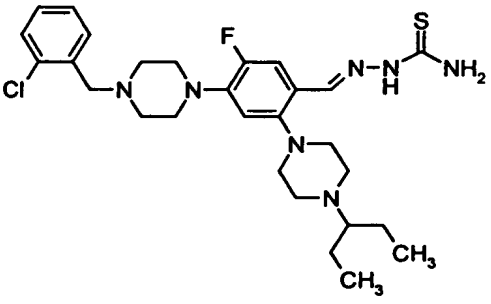
	Structur	Name	MH+
759		5-fluoro-4-[4-(2-fluorobenzoyl)piperazin-1-yl]-2-piperidin-1-ylbenzaldehyde thiosemicarbazone	488
760		1-[4-(trifluoromethyl)benzyl]piperidine-2-carbaldehyde N-(tetrahydrofuran-2-ylmethyl)thiosemicarbazone	430
761		2-{4-[(5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-furyl)methyl]piperazin-1-yl}benzonitrile	369
762		5-(3-methoxyphenyl)-2-furaldehyde thiosemicarbazone	276
763		4-[4-(2-chlorobenzyl)piperazin-1-yl]-2-[4-(1-ethylpropyl)piperazin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	561

TABLE 3

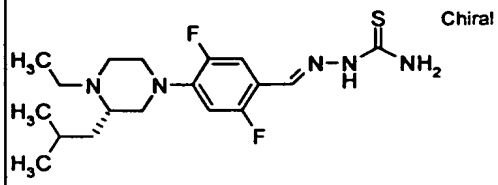
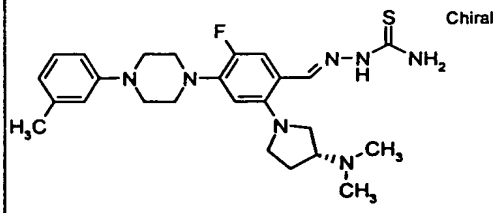
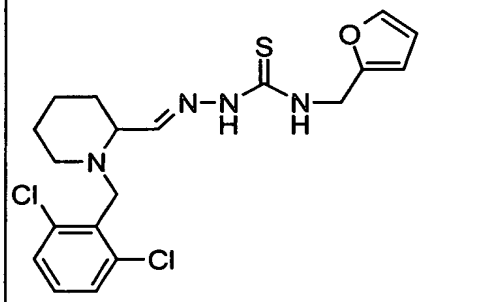
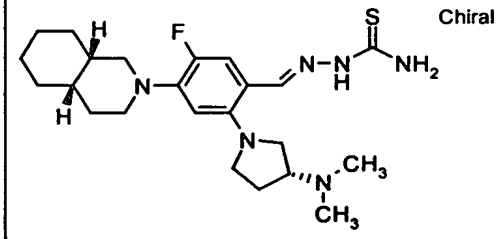
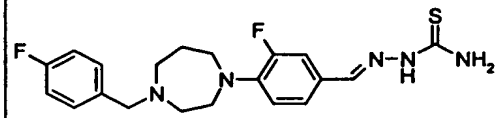
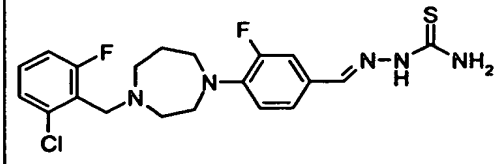
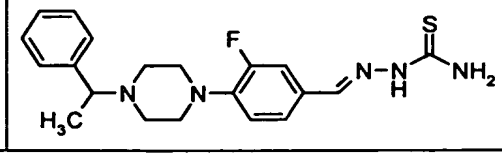
	Structure	Name	MH+
764	 Chiral	4-[(3S)-4-ethyl-3-isobutylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	385
765	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-[4-(3-methylphenyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	485
766		1-(2,6-dichlorobenzyl)piperidine-2-carbaldehyde N-(2-furylmethyl)thiosemicarbazone	426
767	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-[(4aS,8aS)-octahydroisoquinolin-2(1H)-yl]benzaldehyde thiosemicarbazone	448
768		3-fluoro-4-[4-(4-fluorobenzyl)-1,4-diazepan-1-yl]benzaldehyde thiosemicarbazone	404
769		4-[4-(2-chloro-6-fluorobenzyl)-1,4-diazepan-1-yl]-3-fluorobenzaldehyde thiosemicarbazone	439
770		3-fluoro-4-[4-(1-phenylethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	387

TABLE 3

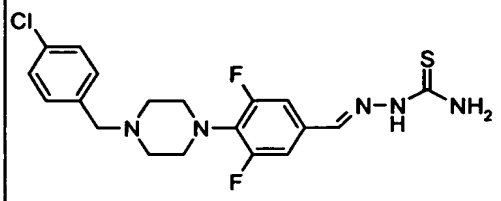
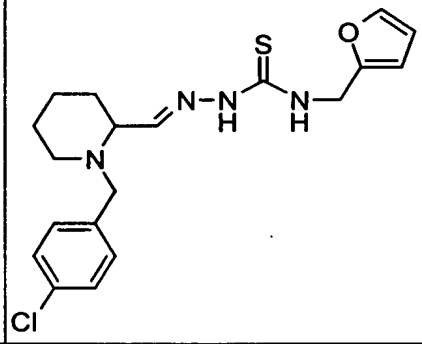
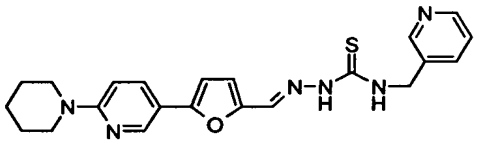
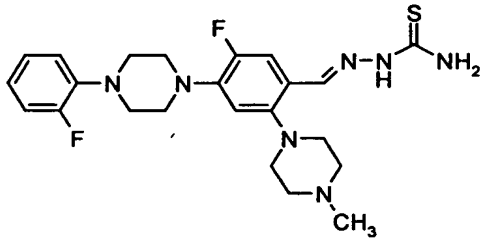
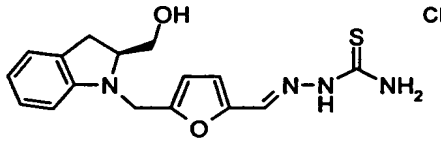
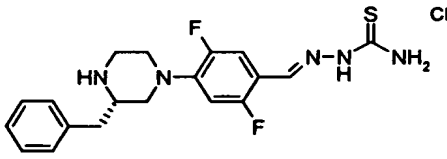
	Structure	Name	MH+
771		4-[4-(4-chlorobenzyl)piperazin-1-yl]-3,5-difluorobenzaldehyde thiosemicarbazone	425
772		1-(4-chlorobenzyl)piperidine-2-carbaldehyde N-(2-furylmethyl)thiosemicarbazone	392
773		5-(6-piperidin-1-ylpyridin-3-yl)-2-furaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone	422
774		5-fluoro-4-[4-(2-fluorophenyl)piperazin-1-yl]-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	475
775	 Chiral	5-{[(2S)-2-(hydroxymethyl)-2,3-dihydro-1H-indol-1-yl]methyl}-2-furaldehyde thiosemicarbazone	331
776	 Chiral	4-[(3S)-3-benzylpiperazin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	390

TABLE 3

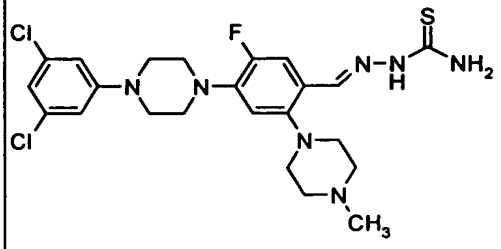
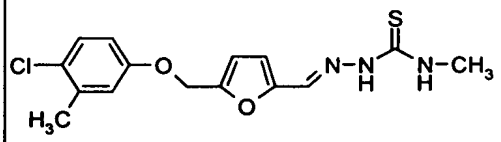
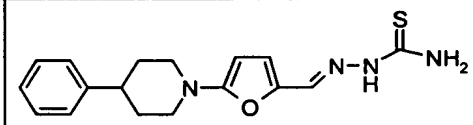
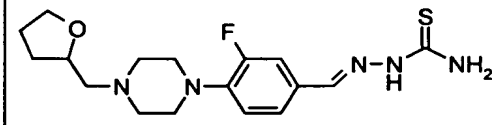
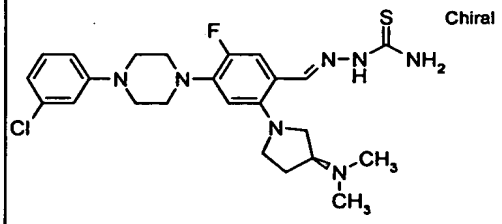
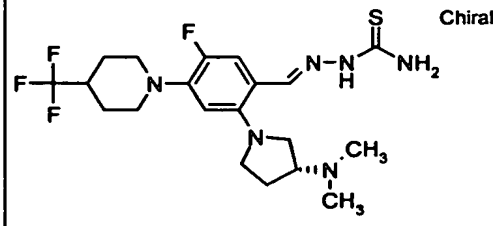
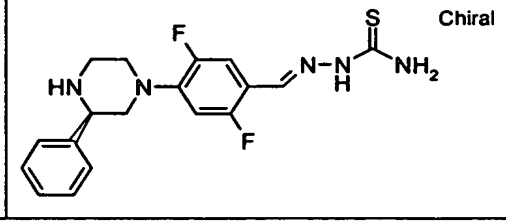
	Structure	Name	MH+
777		4-[4-(3,5-dichlorophenyl)piperazin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	525
778		5-[(4-chloro-3-methylphenoxy)methyl]-2-furaldehyde N-methylthiosemicarbazone	339
779		5-(4-phenylpiperidin-1-yl)-2-furaldehyde thiosemicarbazone	329
780		3-fluoro-4-[4-(tetrahydrofuran-2-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	366
781	 Chiral	4-[4-(3-chlorophenyl)piperazin-1-yl]-2-[(3S)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	505
782	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-[4-(trifluoromethyl)piperidin-1-yl]benzaldehyde thiosemicarbazone	462
783	 Chiral	2,5-difluoro-4-[(3R)-3-phenylpiperazin-1-yl]benzaldehyde thiosemicarbazone	376

TABLE 3

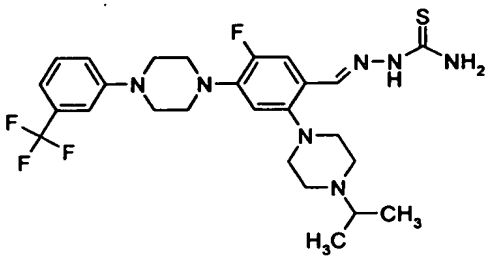
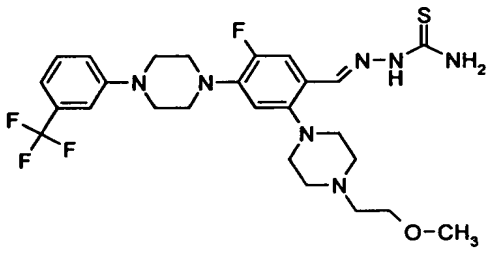
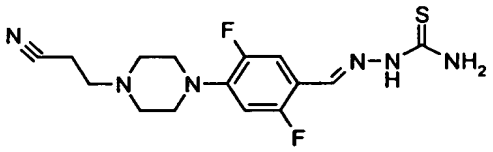
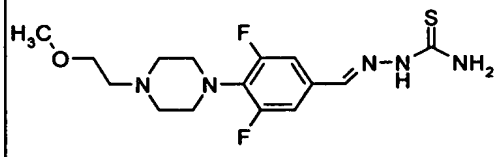
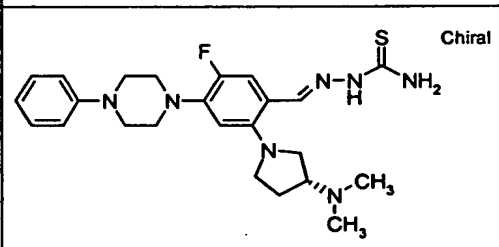
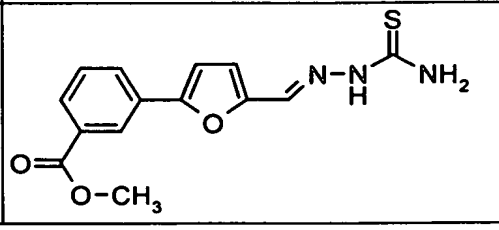
	Structure	Name	MH+
784		5-fluoro-2-(4-isopropylpiperazin-1-yl)-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	553
785		5-fluoro-2-[4-(2-methoxyethyl)piperazin-1-yl]-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	569
786		3-[4-(4-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2,5-difluorophenyl)piperazin-1-yl]propanenitrile	353
787		3,5-difluoro-4-[4-(2-methoxyethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	358
788		2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-(4-phenylpiperazin-1-yl)benzaldehyde thiosemicarbazone	471
789		methyl 3-(5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-furyl)benzoate	304

TABLE 3

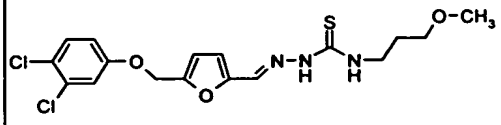
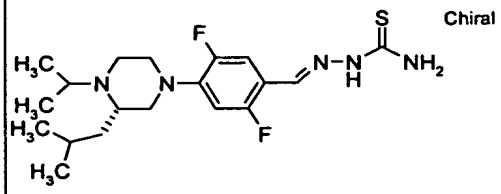
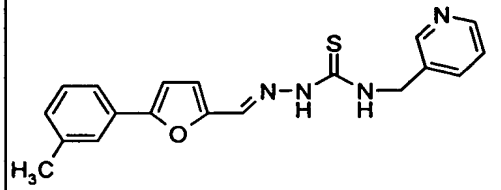
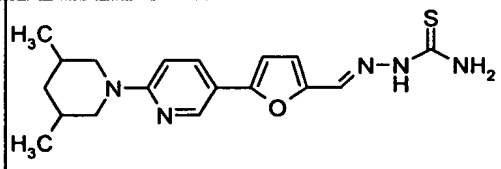
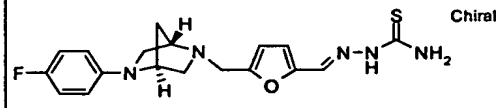
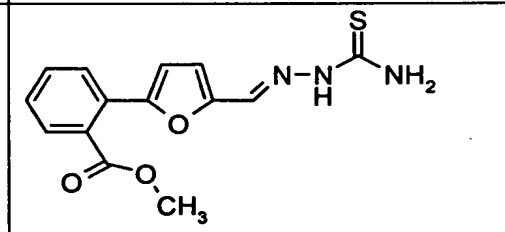
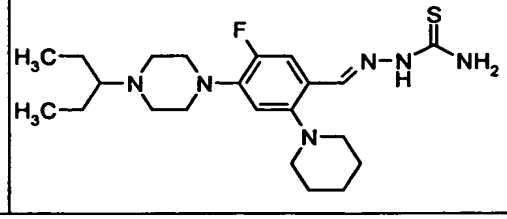
	Structure	Name	MH+
790		5-[(3,4-dichlorophenoxy)methyl]-2-furaldehyde N-(3-methoxypropyl)thiosemicarbazone	417
791		2,5-difluoro-4-[(3S)-3-isobutyl-4-isopropylpiperazin-1-yl]benzaldehyde thiosemicarbazone	399
792		5-(3-methylphenyl)-2-furaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone	351
793		5-[6-(3,5-dimethylpiperidin-1-yl)pyridin-3-yl]-2-furaldehyde thiosemicarbazone	358
794		5-{[(1S,4S)-5-(4-fluorophenyl)-2,5-diazabicyclo[2.2.1]hept-2-yl]methyl}-2-furaldehyde thiosemicarbazone	374
795		methyl 2-(5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-furyl)benzoate	304
796		4-[4-(1-ethylpropyl)piperazin-1-yl]-5-fluoro-2-piperidin-1-ylbenzaldehyde thiosemicarbazone	436

TABLE 3

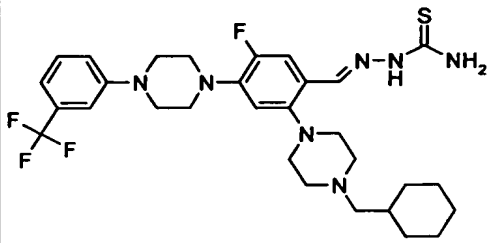
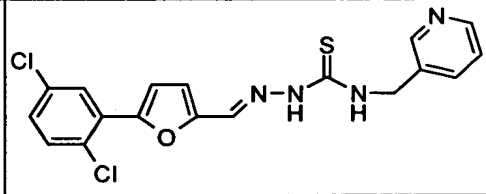
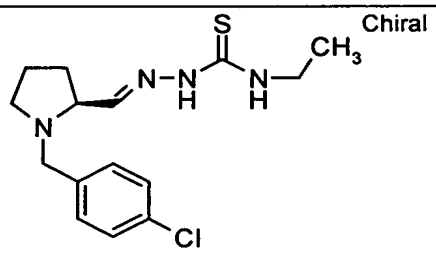
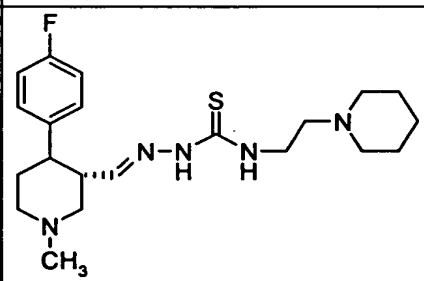
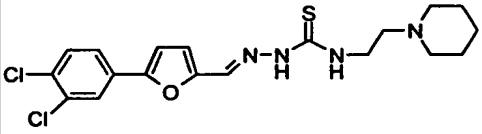
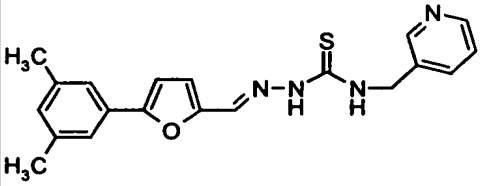
	Structure	Name	MH+
797		2-[4-(cyclohexylmethyl)piperazin-1-yl]-5-fluoro-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	607
798		5-(2,5-dichlorophenyl)-2-furaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone	406
799		(2S)-1-(4-chlorobenzyl)pyrrolidine-2-carbaldehyde N-ethylthiosemicarbazone	326
800		(3S)-4-(4-fluorophenyl)-1-methylpiperidine-3-carbaldehyde N-(2-piperidin-1-ylethyl)thiosemicarbazone	407
801		5-(3,4-dichlorophenyl)-2-furaldehyde N-(2-piperidin-1-ylethyl)thiosemicarbazone	426
802		5-(3,5-dimethylphenyl)-2-furaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone	365

TABLE 3

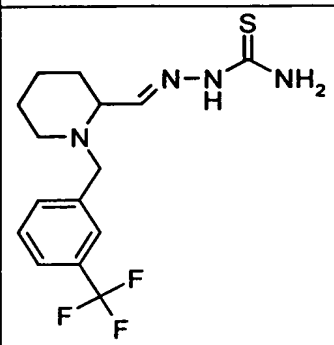
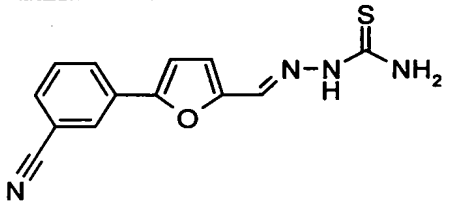
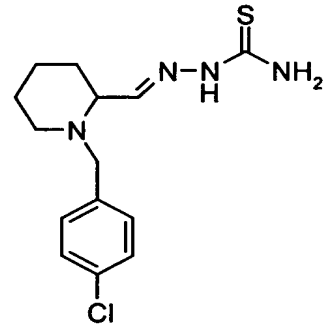
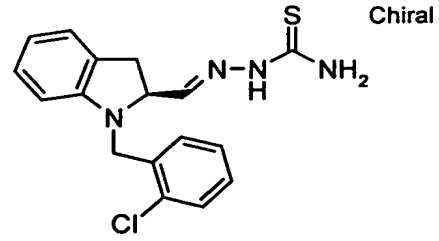
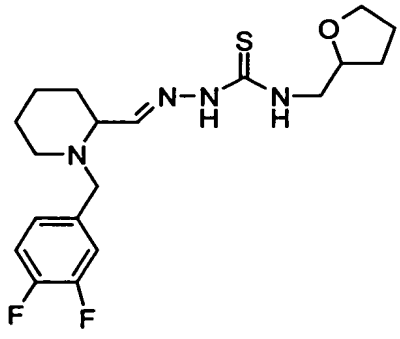
	Structur	Name	MH+
803		1-[3-(trifluoromethyl)benzyl]piperidine-2-carbaldehyde thiosemicarbazone	345
804		3-(5-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-furyl)benzonitrile	271
805		1-(4-chlorobenzyl)piperidine-2-carbaldehyde thiosemicarbazone	312
806		(2S)-1-(2-chlorobenzyl)indoline-2-carbaldehyde thiosemicarbazone	346
807		1-(3,4-difluorobenzyl)piperidine-2-carbaldehyde N-(tetrahydrofuran-2-ylmethyl)thiosemicarbazone	398

TABLE 3

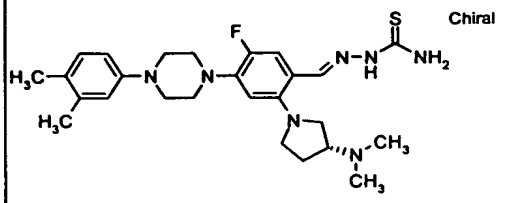
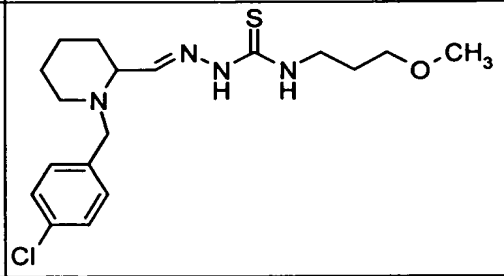
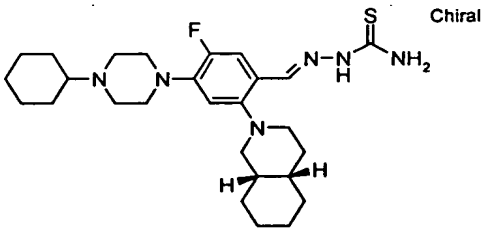
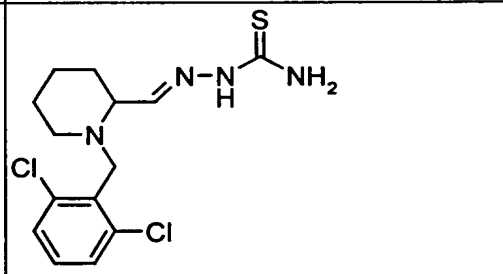
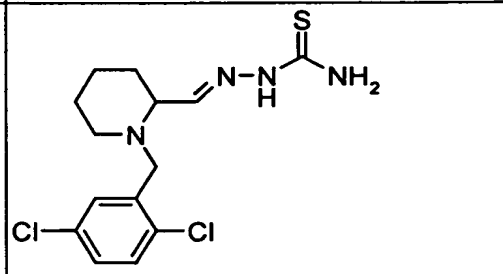
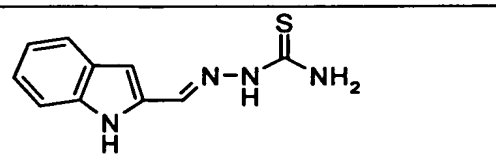
	Structure	Name	MH+
808	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-4-[4-(3,4-dimethylphenyl)piperazin-1-yl]-5-fluorobenzaldehyde thiosemicarbazone	499
809		1-(4-chlorobenzyl)piperidine-2-carbaldehyde N-(3-methoxypropyl)thiosemicarbazone	384
810	 Chiral	4-(4-cyclohexylpiperazin-1-yl)-5-fluoro-2-[(4aS,8aS)-octahydroisoquinolin-2(1H)-yl]benzaldehyde thiosemicarbazone	502
811		1-(2,6-dichlorobenzyl)piperidine-2-carbaldehyde thiosemicarbazone	346
812		1-(2,5-dichlorobenzyl)piperidine-2-carbaldehyde thiosemicarbazone	346
813		1H-indole-2-carbaldehyde thiosemicarbazone	219

TABLE 3

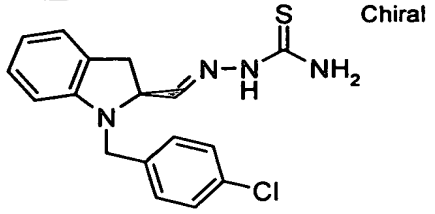
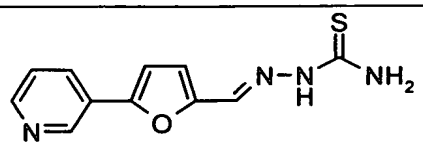
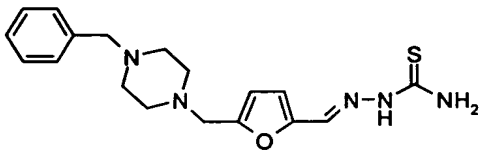
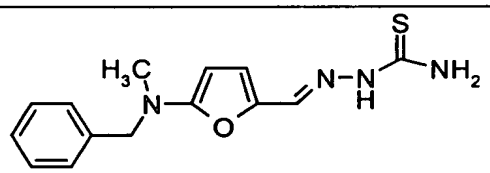
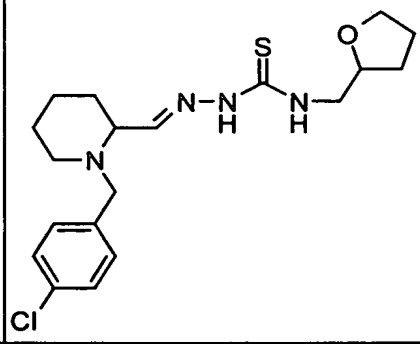
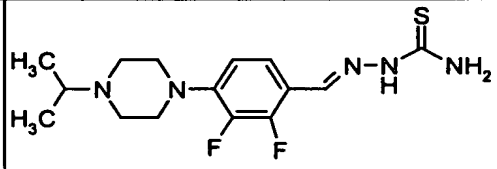
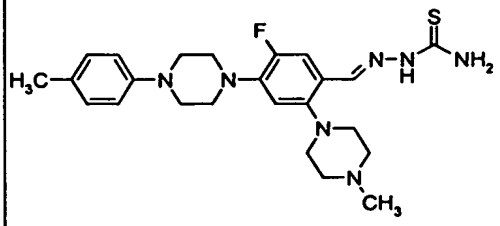
	Structure	Name	MH+
814	 Chiral	(2S)-1-(4-chlorobenzyl)indoline-2-carbaldehyde thiosemicarbazone	346
815		5-pyridin-3-yl-2-furaldehyde thiosemicarbazone	247
816		5-[(4-benzylpiperazin-1-yl)methyl]-2-furaldehyde thiosemicarbazone	358
817		5-[benzyl(methyl)amino]-2-furaldehyde thiosemicarbazone	289
818		1-(4-chlorobenzyl)piperidine-2-carbaldehyde N-(tetrahydrofuran-2-ylmethyl)thiosemicarbazone	396
819		2,3-difluoro-4-(4-isopropylpiperazin-1-yl)benzaldehyde thiosemicarbazone	342
820		5-fluoro-4-[4-(4-methylphenyl)piperazin-1-yl]-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	471

TABLE 3

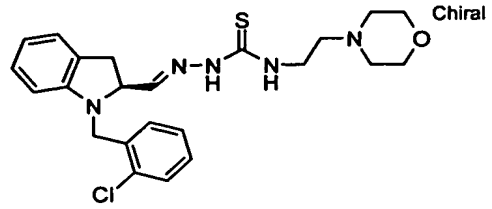
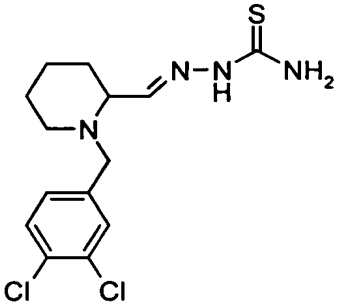
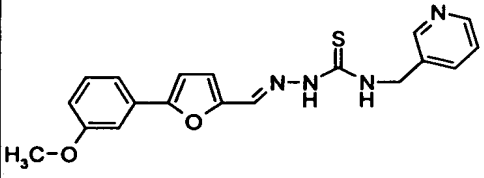
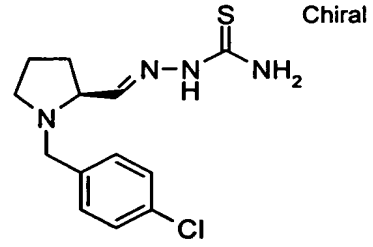
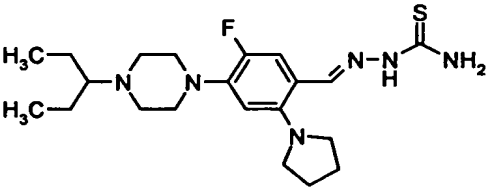
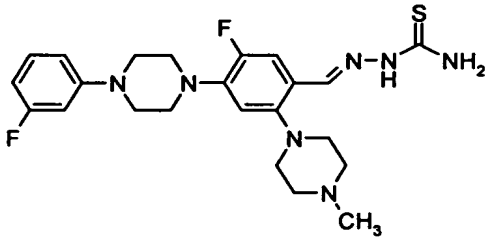
	Structure	Name	MH+
821		(2S)-1-(2-chlorobenzyl)indoline-2-carbaldehyde N-(2-morpholin-4-ylethyl)thiosemicarbazone	459
822		1-(3,4-dichlorobenzyl)piperidine-2-carbaldehyde thiosemicarbazone	346
823		5-(3-methoxyphenyl)-2-furaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone	367
824		(2S)-1-(4-chlorobenzyl)pyrrolidine-2-carbaldehyde thiosemicarbazone	298
825		4-[4-(1-ethylpropyl)piperazin-1-yl]-5-fluoro-2-pyrrolidin-1-ylbenzaldehyde thiosemicarbazone	422
826		5-fluoro-4-[4-(3-fluorophenyl)piperazin-1-yl]-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	475

TABLE 3

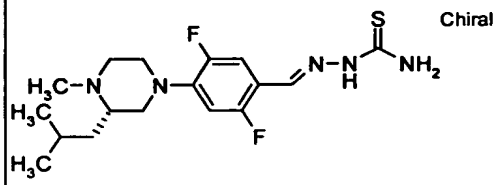
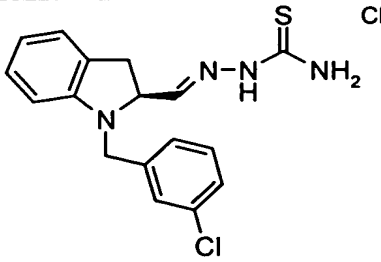
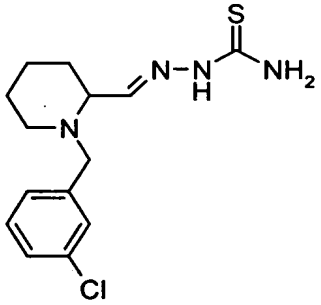
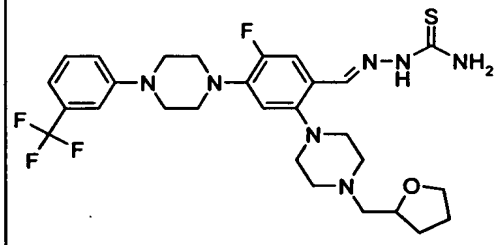
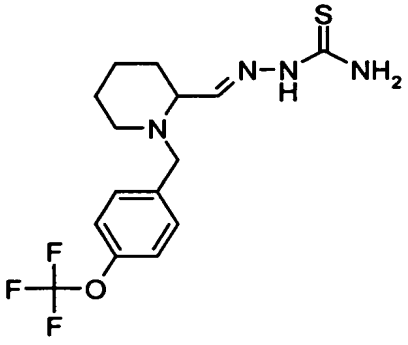
	Structure	Name	MH+
827	 Chiral	2,5-difluoro-4-[(3S)-3-isobutyl-4-methylpiperazin-1-yl]benzaldehyde thiosemicarbazone	370
828	 Chiral	(2S)-1-(3-chlorobenzyl)indoline-2-carbaldehyde thiosemicarbazone	346
829		1-(3-chlorobenzyl)piperidine-2-carbaldehyde thiosemicarbazone	312
830		5-fluoro-2-[4-(tetrahydrofuran-2-ylmethyl)piperazin-1-yl]-4-{4-[3-(trifluoromethyl)phenyl]piperazin-1-yl}benzaldehyde thiosemicarbazone	595
831		1-[4-(trifluoromethoxy)benzyl]piperidine-2-carbaldehyde thiosemicarbazone	361

TABLE 3

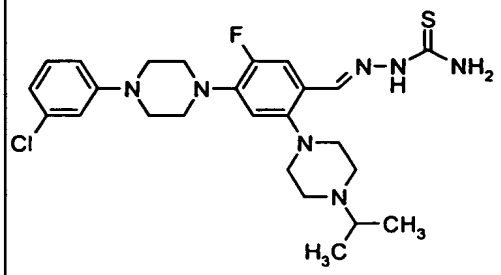
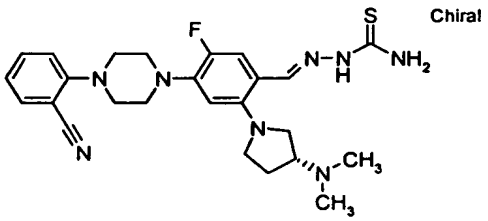
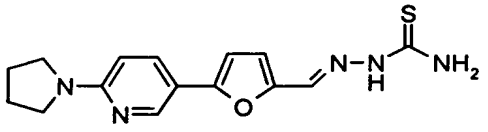
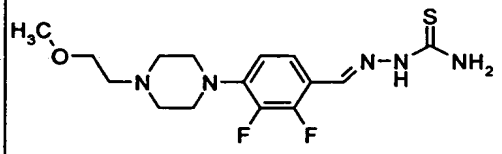
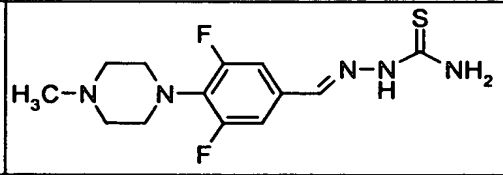
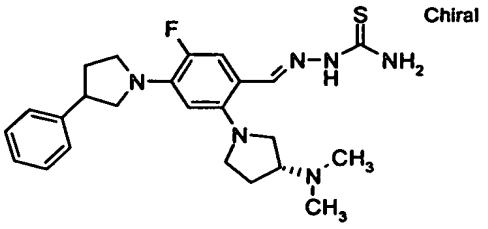
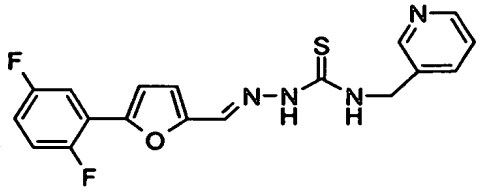
	Structur	Name	MH+
832		4-[4-(3-chlorophenyl)piperazin-1-yl]-5-fluoro-2-(4-isopropylpiperazin-1-yl)benzaldehyde thiosemicarbazone	519
833	 Chiral	2-(4-{4-[(E)-[(aminocarbonothioyl)hydrazono]methyl}-5-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-2-fluorophenyl}piperazin-1-yl)benzonitrile	496
834		5-(6-pyrrolidin-1-ylpyridin-3-yl)-2-furaldehyde thiosemicarbazone	316
835		2,3-difluoro-4-[4-(2-methoxyethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	358
836		3,5-difluoro-4-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	314
837	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-(3-phenylpyrrolidin-1-yl)benzaldehyde thiosemicarbazone	456
838		5-(2,5-difluorophenyl)-2-furaldehyde N-(pyridin-3-ylmethyl)thiosemicarbazone	373

TABLE 3

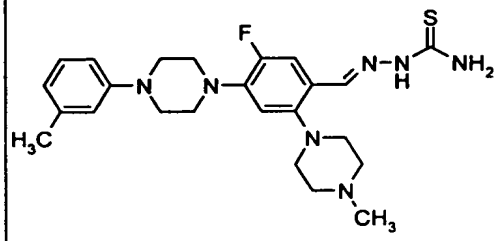
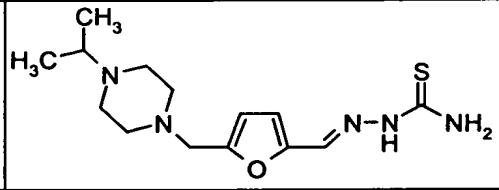
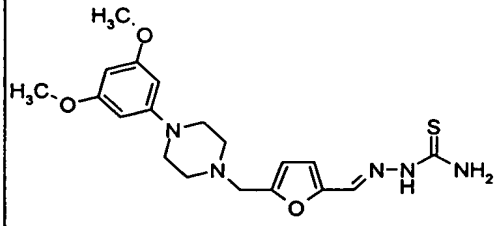
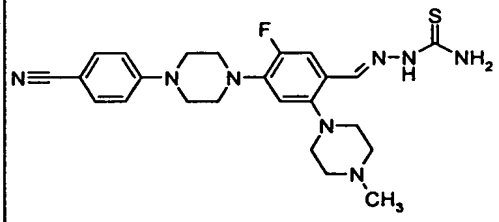
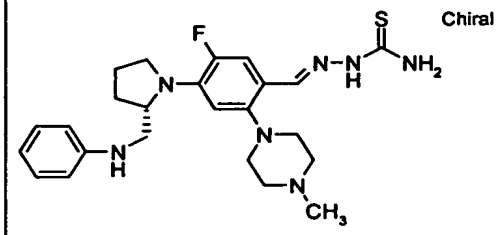
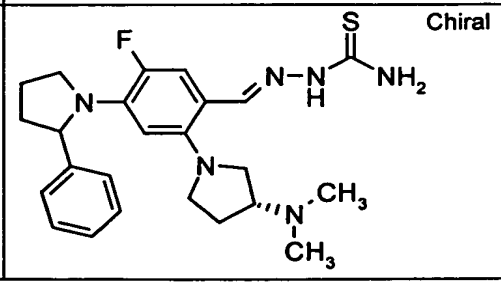
	Structure	Name	MH+
839		5-fluoro-4-[4-(3-methylphenyl)piperazin-1-yl]-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	471
840		5-[(4-isopropylpiperazin-1-yl)methyl]-2-furaldehyde thiosemicarbazone	310
841		5-{[4-(3,5-dimethoxyphenyl)piperazin-1-yl]methyl}-2-furaldehyde thiosemicarbazone	405
842		4-{4-[4-{(E)-[(aminocarbonothioyl)hydrazono]methyl}-2-fluoro-5-(4-methylpiperazin-1-yl)phenyl]piperazin-1-yl}benzonitrile	482
843	 Chiral	4-[(2S)-2-(anilinomethyl)pyrrolidin-1-yl]-5-fluoro-2-(4-methylpiperazin-1-yl)benzaldehyde thiosemicarbazone	471
844	 Chiral	2-[(3R)-3-(dimethylamino)pyrrolidin-1-yl]-5-fluoro-4-(2-phenylpyrrolidin-1-yl)benzaldehyde thiosemicarbazone	456

TABLE 3

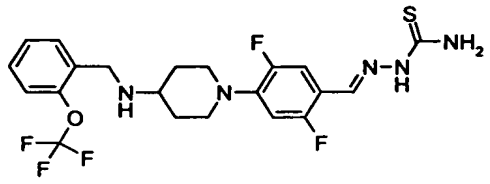
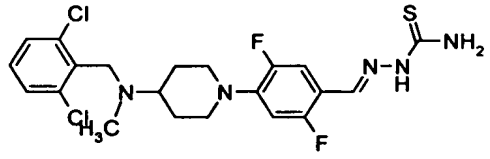
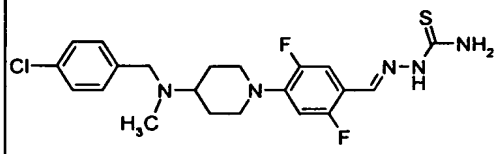
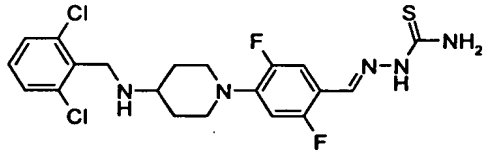
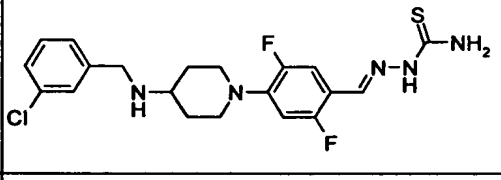
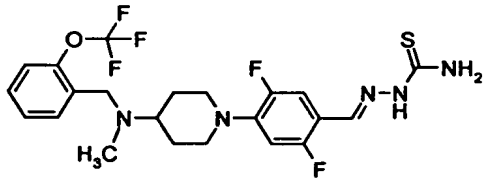
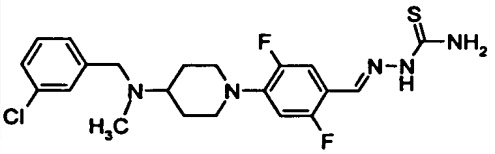
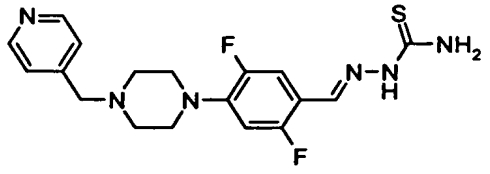
	Structure	Nam	MH+
845		2,5-difluoro-4-(4-{[2-(trifluoromethoxy)benzyl]amino}piperidin-1-yl)benzaldehyde thiosemicarbazone	488
846		4-{4-[(2,6-dichlorobenzyl)(methyl)amino]piperidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	487
847		4-{4-[(4-chlorobenzyl)(methyl)amino]piperidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	453
848		4-{4-[(2,6-dichlorobenzyl)amino]piperidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	473
849		4-{4-[(3-chlorobenzyl)amino]piperidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	439
850		2,5-difluoro-4-(4-{methyl[2-(trifluoromethoxy)benzyl]amino}piperidin-1-yl)benzaldehyde thiosemicarbazone	503
851		4-{4-[(3-chlorobenzyl)(methyl)amino]piperidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	453
852		2,5-difluoro-4-[4-(pyridin-4-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	391

TABLE 3

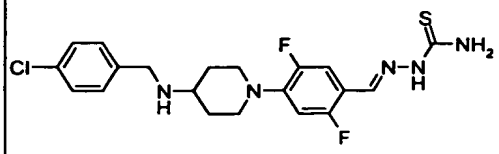
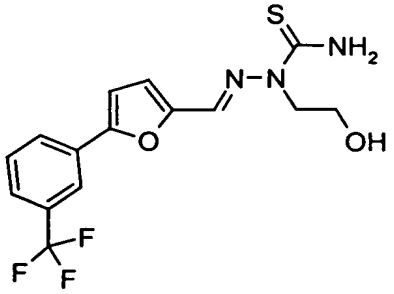
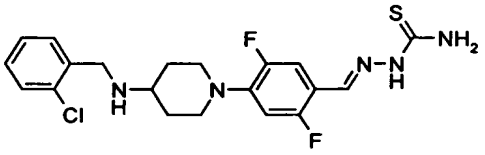
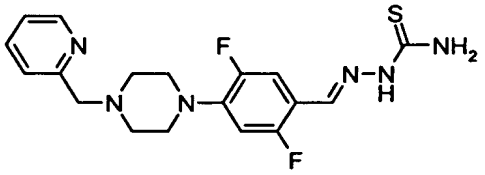
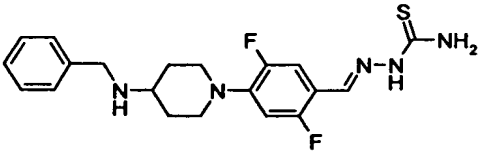
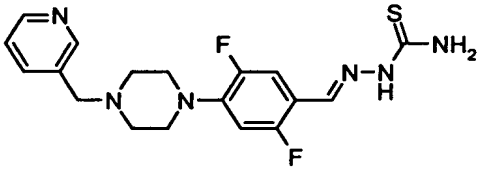
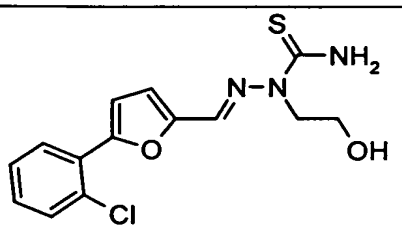
	Structure	Name	MH+
853		4-{4-[(4-chlorobenzyl)amino]piperidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	439
854		5-[3-(trifluoromethyl)phenyl]-2-furaldehyde N'-(2-hydroxyethyl)thiosemicarbazone	358
855		4-{4-[(2-chlorobenzyl)amino]piperidin-1-yl}-2,5-difluorobenzaldehyde thiosemicarbazone	439
856		2,5-difluoro-4-[4-(pyridin-2-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	391
857		4-[4-(benzylamino)piperidin-1-yl]-2,5-difluorobenzaldehyde thiosemicarbazone	404
858		2,5-difluoro-4-[4-(pyridin-3-ylmethyl)piperazin-1-yl]benzaldehyde thiosemicarbazone	391
859		5-(2-chlorophenyl)-2-furaldehyde N'-(2-hydroxyethyl)thiosemicarbazone	325

TABLE 3

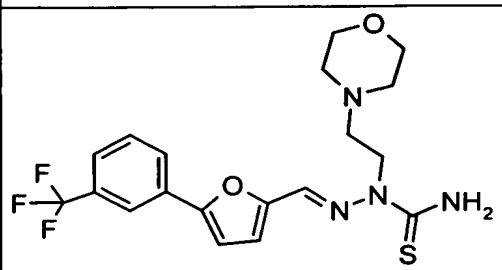
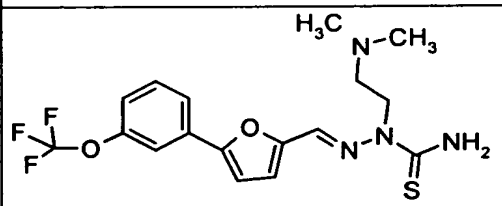
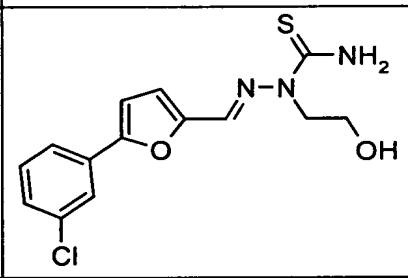
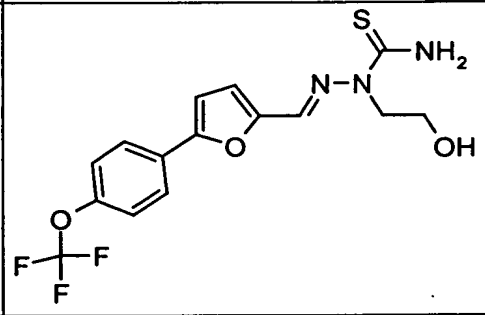
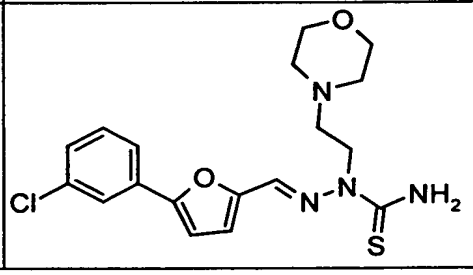
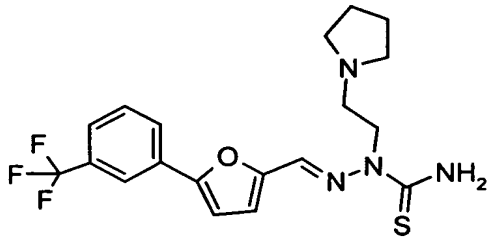
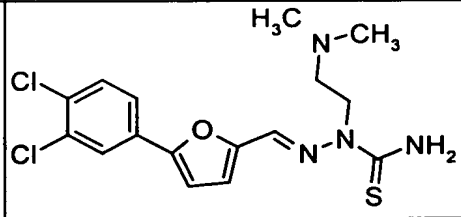
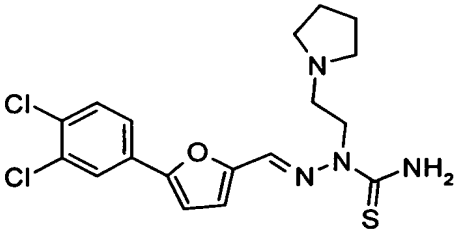
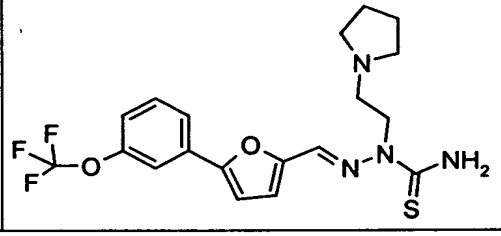
	Structure	Name	MH+
860		5-[3-(trifluoromethyl)phenyl]-2-furaldehyde N'-(2-morpholin-4-ylethyl)thiosemicarbazone	427
861		5-[3-(trifluoromethoxy)phenyl]-2-furaldehyde N'-[2-(dimethylamino)ethyl]thiosemicarbazone	401
862		5-(3-chlorophenyl)-2-furaldehyde N'-(2-hydroxyethyl)thiosemicarbazone	325
863		5-[4-(trifluoromethoxy)phenyl]-2-furaldehyde N'-(2-hydroxyethyl)thiosemicarbazone	374
864		5-(3-chlorophenyl)-2-furaldehyde N'-(2-morpholin-4-ylethyl)thiosemicarbazone	394

TABLE 3

	Structure	Name	MH+
865		5-[3-(trifluoromethyl)phenyl]-2-furaldehyde N'-(2-pyrrolidin-1-ylethyl)thiosemicarbazone	411
866		5-(3,4-dichlorophenyl)-2-furaldehyde N'-[2-(dimethylamino)ethyl]thiosemicarbazone	386
867		5-(3,4-dichlorophenyl)-2-furaldehyde N'-(2-pyrrolidin-1-ylethyl)thiosemicarbazone	412
868		5-[3-(trifluoromethoxy)phenyl]-2-furaldehyde N'-(2-pyrrolidin-1-ylethyl)thiosemicarbazone	427

[0430] The compounds of Table 3 were assayed according to the procedures set forth with regard to Table 1. Each of these Example compounds displayed an IC_{50} value of less than 10 μM with respect to HCV. Many of the compounds displayed an IC_{50} value of less than or equal to 1 μM or less than or equal to 0.1 μM. Many of these compounds exhibited IC_{50} values of less than or equal to 0.050 μM, less than or equal to 0.030 μM, less than or equal to 0.025 μM, or less than or equal to 0.010 μM. Thus, as described above, the compounds are well-suited for use in the methods described herein.

[0431] While the invention has been described with respect to specific examples including presently preferred modes of carrying out the invention, those skilled in the art will

appreciate that there are numerous variations and permutations of the above described systems and techniques that fall within the spirit and scope of the invention.

[0432] Antigen references cited:

[0433] 1. International patent application WO99/24578

[0434] 2. International patent application WO99/36544.

[0435] 3. International patent application WO99/57280.

[0436] 4. International patent application WO00/22430.

[0437] 5. Tettelin et al. (2000) Science 287:1809-1815.

[0438] 6. International patent application WO96/29412.

[0439] 7. Pizza et al. (2000) Science 287:1816-1820.

[0440] 8. International patent application PCT/B01/0066.

[0441] 9. Bjune et al. (1991) Lancet 338(8775).

[0442] 10. Fuskasawa et al. (1999) Vaccine 17:2951-2958.

[0443] 11. Rosenqist et al. (1998) Dev. Biol. Strand 92:323-333.

[0444] 12. Constantino et al. (1992) Vaccine 10:691-698.

[0445] 13. Constantino et al. (1999) Vaccine 17:1251-1263.

[0446] 14. Watson (2000) Pediatr Infect Dis J 19:331-332.

[0447] 15. Rubin (20000) Pediatr Clin North Am 47:269-285,v.

[0448] 16. Jedrzejas (2001) Microbiol Mol Biol Rev 65:187-207.

[0449] 17. International patent application filed on 3rd July 2001 claiming priority from GB-0016363.4].

[0450] 18. Kalman et al. (1999) Nature Genetics 21:385-389.

[0451] 19. Read et al. (2000) Nucleic Acids Res 28:1397-406.

[0452] 20. Shirai et al. (2000) J. Infect. Dis 181(Suppl 3):S524-S527.

[0453] 21. International patent application WO99/27105.

[0454] 22. International patent application WO00/27994.

[0455] 23. International patent application WO00/37494.

[0456] 24. International patent application WO99/28475.

[0457] 25. Bell (2000) Pediatr Infect Dis J 19:1187-1188.

[0458] 26. Iwarson (1995) APMIS 103:321-326.

[0459] 27. Gerlich et al. (1990) Vaccine 8 Suppl:S63-68 & 79-80.

[0460] 28. Hsu et al. (1999) Clin Liver Dis 3:901-915.

[0461] 29. Gastofsson et al. (1996) N. Engl. J. Med. 334-:349-355.

[0462] 30. Rappuoli et al. (1991) TIBTECH 9:232-238.

[0463] 31. Vaccines (1988) eds. Plotkin & Mortimer. ISBN 0-7216-1946-0.

[0464] 32. Del Guidice et al. (1998) Molecular Aspects of Medicine 19:1-70.

[0465] 33. International patent application WO93/018150.

[0466] 34. International patent application WO99/53310.

[0467] 35. International patent application WO98/04702.

[0468] 36. Ross et al. (2001) Vaccine 19:135-142.

[0469] 37. Sutter et al. (2000) Pediatr Clin North Am 47:287-308.

[0470] 38. Zimmerman & Spann (1999) Am Fan Physician 59:113-118, 125-126.

[0471] 39. Dreensen (1997) Vaccine 15 Suppl"S2-6.

[0472] 40. MMWR Morb Mortal Wkly rep 1998 Jan 16:47(1):12, 9.

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